# CHAPTER 7:
# Special topic: Liver cancer

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**Statistics at a glance**

| Incidence (estimates for 2013) | Males | Females |
|---|---|---|
| Number of new cases | 1,550 | 490 |
| Age-standardized rates (per 100,000) | 6.9 | 1.9 |
| % of all cancers | 1.6 | 0.5 |
| **Mortality (estimates for 2013)** | | |
| Number of deaths | 780 | 240 |
| Age-standardized rates (per 100,000) | 3.5 | 0.9 |
| % of all cancers | 2.0 | 0.7 |
| **Survival (2006–2008)** | | |
| Five-year relative survival (%) | 20 | 19 |
| **Prevalence** | | |
| 10-year person-based prevalence (as of Jan 1, 2009) | 2,242 | 743 |
| **Potential years of life lost (2009)** | | |
| Number of years of life lost | 11,200 | 3,500 |

**Note:** Rates are age-standardized to the 1991 Canadian population.

## Highlights

- Liver cancer is one of the fastest rising cancers in Canada. In 2013, over 2,000 Canadians are expected to develop primary liver cancer and about 1,000 will die of this disease.
- Between 1970 and 2007, the incidence rate of liver cancer in Canadian males increased by an average of 3.6% per year. In Canadian females, the rate increased by 2.6% per year between 1986 and 2007.
- The main subtype of liver cancer is hepatocellular carcinoma (HCC).
- The predominant risk factor for liver cancer in Canada is chronic viral hepatitis infection with hepatitis B virus (HBV) or hepatitis C virus (HCV). Alcohol abuse, obesity, diabetes and smoking are also associated with a higher risk and may play an increasingly important role in the growing incidence of liver cancer in Canada.
- The five-year relative survival ratio (RSR) for primary liver cancer is 20%.
- As of January 1, 2009, it is estimated that there were 2,985 Canadians (2,242 males and 743 females) who had been diagnosed with primary liver cancer in the previous 10 years and were still alive on that date.
- Liver cancer is associated with high costs for treatment and managing the disease presents both clinical and financial challenges.
- Several measures can be taken to reduce liver cancer risk, including:
  - preventing infection with HBV and HCV, reducing alcohol intake, and avoiding obesity and smoking
  - identifying and treating cirrhosis and chronic infection with HBV or HCV
  - implementing public education about risk reduction and who should be screened, as well as removing stigma from screening
  - educating healthcare providers about who to screen, screening protocols and how to test and treat the disease

## Epidemiology of liver cancer

In 2013, over 2,000 Canadians are expected to develop primary liver cancer and about 1,000 will die of this disease. While it remains relatively uncommon (accounting for an estimated 1% of all new cancer diagnoses and deaths in 2013), the morbidity and mortality associated with liver cancer have been rising in Canada. In 2009, premature death from liver cancer caused 14,700 potential years of life lost (PYLL), which represented 1.3% (2.1% in males and 0.6% in females) of all PYLL due to cancer in Canada.

**Potential years of life lost (PYLL)**

An estimate of the number of years of life lost due to premature death. It provides an alternative measure to death rates by taking into account average life expectancy and giving more weight to deaths that occur among younger people.

The liver performs many functions. It produces bile, processes nutrients and drugs, and filters blood from the stomach and intestines. Other liver functions include removing and excreting body waste, synthesizing plasma proteins and helping the body fight infection.

Primary liver cancer originates in cells of the liver (hepatocytes), bile ducts or blood vessels or connective tissue of the liver. However, the liver is also a frequent site for metastatic cancer. Metastatic cancer in the liver occurs when cancer cells from tumours in other parts of the body, such as the lung, breast, pancreas, gastrointestinal tract or lymphatic system, travel to the liver through the blood or lymph fluid. These cancer cells can establish tumours in the liver. Histopathology and the radiologic characteristics of a tumour can help determine whether cancer in the liver is primary or metastatic. This chapter focuses on primary (i.e., non-metastatic) liver cancer.

Hepatocellular carcinoma (HCC) and cholangiocarcinoma are the two main morphologic types of liver cancer in adults. As shown in Table 7.1:

- HCC develops from hepatocytes and accounts for the majority (71.9%) of liver cancers in males and females in Canada.
- Cholangiocarcinoma develops from the epithelial lining of the intrahepatic bile ducts. It is less common than HCC, accounting for 4.1% of liver cancers in Canada.
- In children, hepatoblastoma is the most common hepatic tumour, accounting for 1.1% of all new liver cancer cases.
- A large proportion of liver cancer diagnoses are classified as "unspecified" and some of these are likely to be HCC.

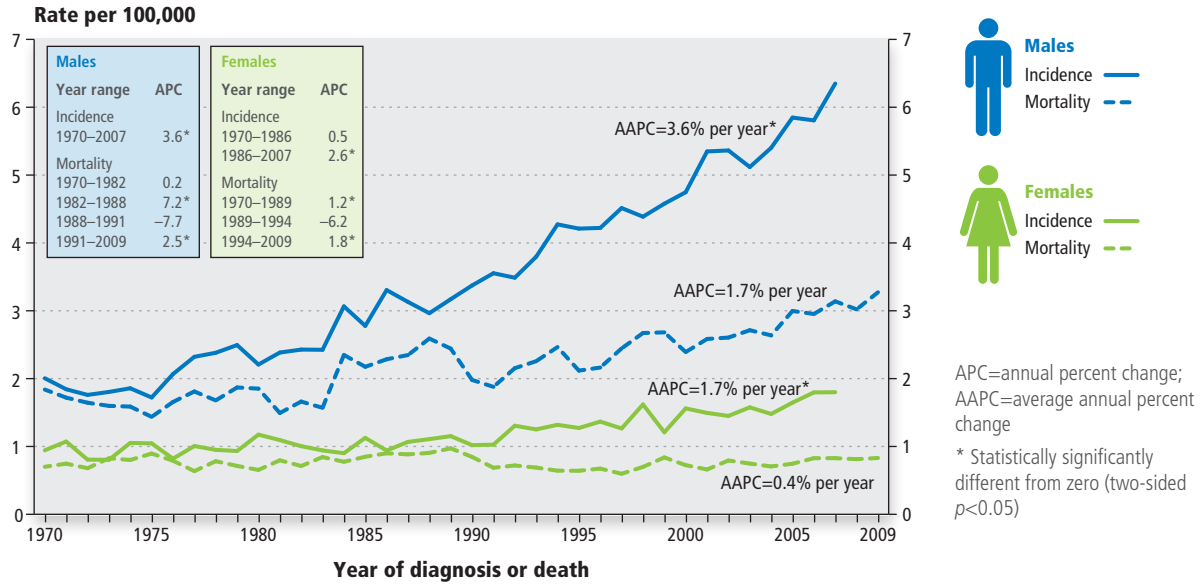
Because most adult liver cancer cases are HCC, the majority of this chapter focuses on this morphologic type.

## Age and sex differences in incidence and mortality rates

Age-standardized incidence rates (ASIR) for primary liver cancer for both males and females in Canada have increased in the past four decades (Figure 7.1).

- The incidence rate is higher in males. Between 1970 and 2007, this rate tripled from 2.0 to 6.3 per 100,000. This represents an average annual percent change (AAPC) of 3.6% per year.
- Between 1970 and 2007, the incidence rate in females doubled from 0.9 to 1.8 per 100,000. The fastest increase occurred between 1986 and 2007, where the incidence rate increased by an annual percent change (APC) of 2.6% per year.
- Between 1970 and 2009, age-standardized mortality rates (ASMR) for liver cancer also increased from 1.8 to 3.3 per 100,000 in males and 0.7 to 0.8 per 100,000 in females. APCs in the most recent period were 2.5% per year in males since 1991 and 1.8% per year in females since 1994. The increase in incidence and mortality rates have occurred for all groups aged 40 years and older.[1]
- Among Canadian provinces, age-standardized incidence and mortality rates for liver cancer are highest in British Columbia, Alberta, Ontario and Quebec (see *Chapters 2* and *4*).

**FIGURE 7.1** Age-standardized incidence rates (1970–2007) and mortality rates (1970–2009) for primary liver cancer, Canada




**Analysis by:** Chronic Disease Surveillance and Monitoring Division, CCDP, Public Health Agency of Canada
**Data sources:** Canadian Cancer Registry and Canadian Vital Statistics Death databases at Statistics Canada

### International differences in incidence and mortality rates

- Much of the information on the global distribution of cancer comes from the GLOBOCAN 2008 database.[2] This database is a repository of data from cancer registries and other sources and is maintained by the International Agency for Research on Cancer. Worldwide, liver cancer was the sixth most common cancer and accounted for 5.9% of all new cancers in 2008.
- Because HCC is the predominant type of liver cancer in most countries, the global variations in the disease generally reflect trends in HCC incidence and the prevalence of risk factors for HCC. The incidence of HCC is high in Asia, southern Europe and sub-Saharan Africa. The incidence of HCC is lower, but increasing, in North America and parts of Europe.
- As in Canada, the worldwide incidence rate of liver cancer is higher in males than in females. Liver cancer has a very poor prognosis and ranks third in cancer mortality worldwide, accounting for about 700,000 or 9.2% of all cancer-related deaths annually.[2]

## Risk factors

HCC is often preceded by cirrhosis (scarring) of the liver. Cirrhosis can be caused by chronic hepatitis infection, excessive and prolonged use of alcohol, aflatoxin exposure, diabetes, obesity and metabolic disorders that cause liver damage (such as alpha-1 antitrypsin deficiency or hereditary tyrosinemia). Some people with liver cancer have no known risk factors. Trends in liver cancer in Canada strongly reflect the historical and ongoing trends in hepatitis B virus (HBV) and hepatitis C virus (HCV) infections, which are the major risk factors for the disease in this country.

**Age-standardized incidence rate (ASIR)**

The number of new cases of cancer per 100,000 people, standardized to the age structure of the 1991 Canadian population to account for changes in age distribution over time.

**Age-standardized mortality rate (ASMR)**

The number of cancer deaths per 100,000 people, standardized to the age structure of the 1991 Canadian population to account for changes in age distribution over time.

**Annual percent change (APC)**

The estimated change in the rate of new cases or deaths from one year to the next over a defined period of time, reported as a percentage. Along with the changepoint (the year in which the APC changed), the APC is useful for examining trends.

**Average annual percent change (AAPC)**

The average rate of change in a rate over the full period of time being examined. It is a weighted average of the APCs for the full period.

### Hepatitis B

HBV infection accounts for approximately 23% of all HCC cases in developed countries. The percentage of HCC cases related to HBV infection is much higher in the developing world, including in Asia and sub-Saharan Africa.[3] The Public Health Agency of Canada has estimated that chronic carriers of HBV, represent 0.7% to 0.9% of the Canadian population.[4] HBV infection in Canada is linked to increasing immigration from areas of the world where HBV infection is endemic,[5] which is in part reflected by the higher rates of HCC in provinces where most immigrants settle. Most infections in the developing world are transmitted from mother to child at birth. Worldwide, the virus is also commonly passed through exposure to contaminated blood or body fluids between sexual partners and injecting drug users or through other contact with infected individuals.[6] As an oncogenic virus, HBV can lead to HCC without the development of cirrhosis.

### Hepatitis C

Chronic HCV infection accounts for approximately 30% to 50% of HCC cases in North America.[7] Based on statistical models,[8] the prevalence of HCV in Canada is estimated to be 0.7%, but it could be even higher. HCV infection is believed to be associated with exposure to contaminated blood. Individuals at high risk for HCV infection include former or current drug users, immigrants from HCV-endemic regions (e.g., Egypt, Japan, Italy, Pakistan, Bangladesh and Somalia),[9] people occupationally exposed to contaminated blood, Aboriginal people and recipients of transfused blood products prior to the implementation of enhanced blood screening for HCV in Canada in the early 1990s.[10] The majority of immigrants likely acquire HCV infection through unsafe injections or medical procedures in their countries of origin.[11] In the US, baby boomers born in North America between 1945 and 1965 have also been identified as a group at higher than average risk for HCV infection because of the potential for past exposures to HCV.[12]

### Alcohol, obesity, smoking, diabetes and other factors

In the US and northern Europe, more than half of HCC cases are not linked to HBV or HCV,[13] implying that other risk factors may play a role. These risk factors include alcohol-related cirrhosis of the liver,[14] fatty liver disease (steatohepatitis) associated with obesity,[15] smoking[16] and diabetes.[17] Some of these risk factors appear to work as cofactors with liver disease to increase the risk of cancer. For example, in the presence of liver disease, the attributable risk of smoking ranges up to 47%.[18] Alcoholic cirrhosis is thought to be a major risk factor for HCC in areas where prevalence of HBV and HCV is low.[19]

Less common risks include metabolic diseases that cause abnormal liver deposits (e.g., hereditary hemochromatosis, alpha-1 antitrypsin deficiency), primary biliary cirrhosis and autoimmune hepatitis.[20] Oral contraceptive use was previously linked to a higher risk of liver cancer, but the risk associated with newer, low-dose formulations is unclear. In occupational settings, exposure to polychlorinated biphenyls (PCBs)[21] or vinyl chloride[22] has been linked to a higher risk of liver cancer, but exposure to these chemicals is now strictly regulated.

## Diagnosis, treatment, survival and prevalence

### Diagnosis

In most cases, HCC does not cause any symptoms until very late in the course of disease. Although HCC causes bleeding in some cases, it does not cause bleeding into a hollow organ, like colorectal or cervical cancer. Furthermore, it does not present with a palpable mass, such as breast cancer. Diagnosing and caring for people with HCC may also be complicated by the presence of an underlying cirrhosis. Thus, people with liver cancer frequently present with large, late-stage tumours that are often beyond the reach of curative therapy. People with liver cancer may present with acute liver failure, jaundice, ascites, variceal bleeding or hepatic encephalopathy. They may also present with constitutional symptoms of cancer, such as weight loss, night sweats and fatigue. Alternatively, the presentation may be abdominal pain.

Routine screening with ultrasound in people with chronic viral hepatitis, cirrhosis or both may identify asymptomatic, early-stage liver cancer that is amenable to treatment. Early treatment can lead to improved survival.

### Treatment

Several treatment modalities have proven effective against HCC. Many other treatments for which proof of efficacy is lacking are nonetheless used. Resection, radiofrequency ablation (RFA) and liver transplantation are considered potentially curative treatments. All other forms of treatment are considered palliative. HCC is a very uncommon tumour in children and there are no specific strategies for treatment in this age group. Most approaches applied to adults are also applicable to younger people with liver cancer.

The Canadian Association for Study of the Liver,[23] the American Association for Study of Liver Disease[24] and the European Association for Study of the Liver[25] all have similar practice guidelines for managing HCC. As shown in Table 7.2, treatment of HCC depends on the stage of the disease and the health of the liver.[26] In addition to stage and liver status, the selection of treatment is based on the availability of healthcare resources and the level of practitioner expertise.[27]

**Observed survival**

The proportion of people with cancer who are alive after a given period of time (e.g., five years) after diagnosis.

Very early stage HCC is currently difficult to diagnose because it is a single, asymptomatic lesion measuring less than 2 cm in diameter, with no vascular or distant metastases.[27] Surgical resection is considered for very early stage HCC because it is associated with an overall observed survival rate of 90%.[28] RFA is also offered — typically to people whose liver disease or general health precludes surgery — but it has a lower five-year observed survival than surgical resection.

The most appropriate treatment for people with early stage HCC may include either liver resection or liver transplantation, depending on individual and tumour factors, as well as on the status of the underlying liver disease. People with solitary early HCC and well-preserved liver function (Child-Pugh class A) may be treated with liver resection or liver transplantation, although liver resection is favoured in many centres due to the scarcity of donor organs. Liver transplantation is the favoured treatment modality for people with solitary HCC and poor liver function or

multifocal HCC. Liver transplantation is a recognized treatment for people with HCC, but many factors are associated with an increased risk of post-transplant recurrence, including large or multiple lesions, vascular invasion, poorly differentiated histology and an elevated alpha-fetoprotein (over 400 ng/mL). People with early stage HCC who are not candidates for or decline transplant may be offered resection or RFA, depending on the number and size of tumours and liver function status.

For intermediate stage HCC, transarterial chemoembolization (TACE) improves two-year observed survival rate by 20% to 25% compared to more conservative therapy.[28]

For advanced stage HCC with well-preserved liver function (Child-Pugh class A), the primary treatment option is chemotherapy with sorafenib, an oral molecular targeted agent.[28] Unfortunately, many people with advanced HCC and poor liver function are not suitable candidates for any active treatment.

**Five-year relative survival ratio (RSR)**

A measure of the impact of cancer on life expectancy that compares the survival of people diagnosed with cancer to the survival of a comparable group of people in the general population. For example, a five-year RSR of 20% means that the cancer reduces the likelihood of surviving five years after a cancer diagnosis by 80%. Five-year RSR is the preferred measure for assessing population-based cancer survival.

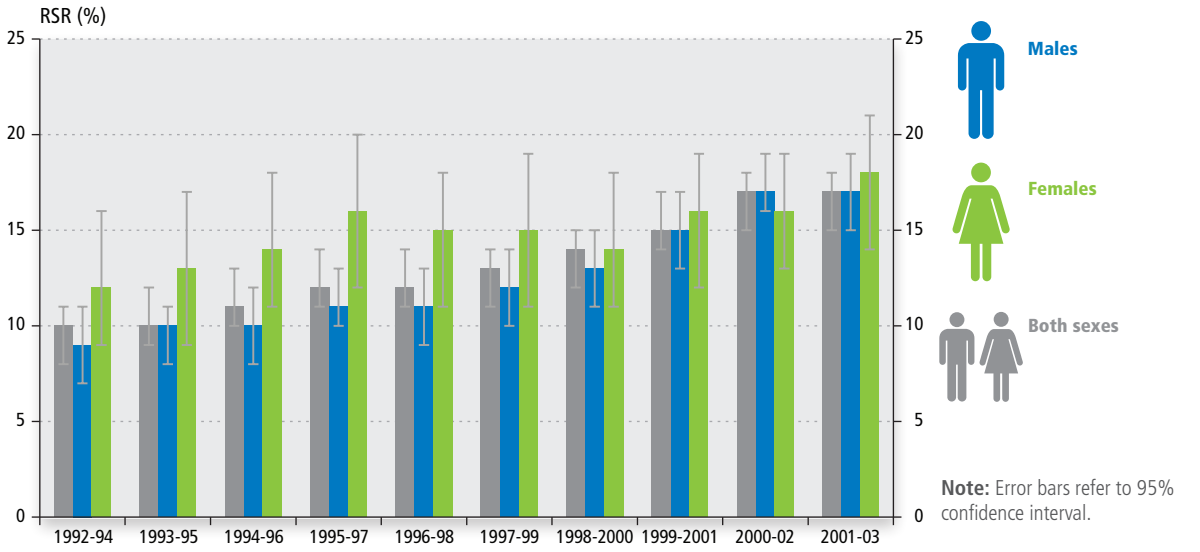
## Survival

Table 7.3 shows that the five-year relative survival ratio (RSR) for liver cancer is 20%, but it differs according to age and stage at diagnosis. As with most other cancer types, survival decreases with advancing age at diagnosis. The greatest difference in survival between the sexes is in people aged 15 to 59 years, where females had better five-year RSRs. Survival data for liver cancer by stage are not currently available for all of Canada. However, data from the US Surveillance Epidemiology and End Results program from 2002 to 2008 indicate that the five-year RSR for liver and intrahepatic bile duct cancer improves dramatically when it is diagnosed at an earlier stage. This program reported the following RSRs by stage: localized stage was 27.7%; regional stage was 10.1%; distant stage was 2.7%; and unknown stage was 6.0%.[29]

In spite of the low RSR compared to other cancer types, the age-standardized five-year RSR for both sexes combined increased from 10% between 1992 and 1994 to 17% between 2001 and 2003 (Figure 7.2). A similar trend occurred in the US, where the increasing RSR is thought to be due to more people being diagnosed at earlier stages as a result of increasing awareness and screening in people at risk for liver cancer.[30] Improvements in diagnosis may also be attributed to the widespread use of ultrasound and measurement of alpha-fetoprotein since the 1980s.[31]

Despite advances in liver cancer treatment,[32] improvements in survival worldwide have not been equally distributed among all social classes. Studies in Korea,[33] the United States[34] and Canada[35] have shown that people with a higher socio-economic status (SES) have better survival outcomes compared to those

**FIGURE 7.2** Age-standardized five-year relative survival ratios (RSRs) by sex, Canada, 1992–2003




**Analysis by:** Health Statistics Division, Statistics Canada
**Data sources:** Canadian Cancer Registry and Canadian Vital Statistics Death databases and life tables at Statistics Canada

with the lowest SES. This association is most likely due to lower income groups being less likely to receive potentially curative treatment.[35] People in lower income groups may also be more likely to present with more advanced disease, which precludes curative therapy. This explanation would be more in keeping with data on other cancers for which effective treatment relies on early diagnosis.

In Ontario between 1990 and 2009, for example, people from the lowest income quintile were less likely to receive curative treatment (25.3% for the lowest income quintile vs. 30.5% to 32.6% for higher income quintiles).[35] As shown in Table 7.4, the median survival durations among those receiving potentially curative therapy, non-curative therapy, palliative therapy and no treatment were 44.4, 21.4, 8.8 and 4.2 months, respectively. The median survival durations for income quintiles 1 to 5 were 8.5, 8.9, 10.5, 10.4 and 8.8 months, respectively.

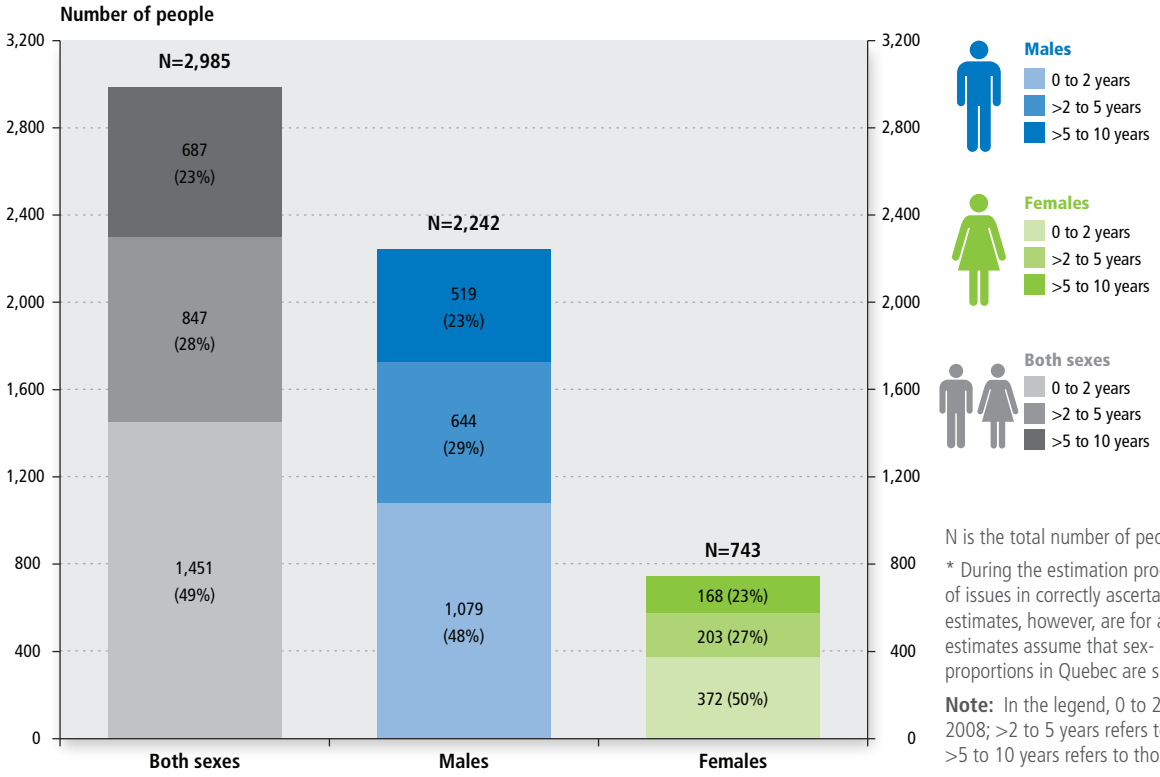
Adjusted hazard ratios suggested that a 10% HCC survival advantage exists for the higher SES groups. This association between SES and HCC survival most likely reflects a lack of access to care for low SES groups, revealing inequities in the Canadian healthcare system.

## Prevalence

As of January 1, 2009, it is estimated that 2,985 Canadians (2,242 males and 743 females) had been diagnosed with primary liver cancer in the previous 10 years and were still alive on that date. Figure 7.3 shows the recency of their diagnosis (i.e., within the past 2 years, between 2 and 5 years ago and between 5 and 10 years ago). The relatively small percentage of people diagnosed between 5 and 10 years ago reflects the poor survival associated with this cancer.

One study estimated that the prevalence proportion of liver cancer cases among Canadian males was highest among those aged 70–79 years, followed by males aged 60–69 years and 80 years and older.[36] These patterns in prevalence reflect the late age at diagnosis of most cases. The prevalence proportion of liver cancer cases has been increasing in Canada. Between 2002 and 2008, the APC was 8.5%, more than double that of any other cancer type examined except thyroid.[37]

**FIGURE 7.3** Person-based prevalence of primary liver cancer by duration and sex, Canada*, January 1, 2009




N is the total number of people with the cancer.

* During the estimation process, cases from Quebec were excluded because of issues in correctly ascertaining the vital status of cases. The presented estimates, however, are for all of Canada, including Quebec. These estimates assume that sex- and age-specific person-based prevalence proportions in Quebec are similar to the rest of Canada.

**Note:** In the legend, 0 to 2 years refers to those diagnosed in 2007 and 2008; >2 to 5 years refers to those diagnosed between 2004 and 2006; >5 to 10 years refers to those diagnosed between 1999 and 2003.

**Analysis by:** Health Statistics Division, Statistics Canada
**Data sources:** Canadian Cancer Registry and Canadian Vital Statistics Death databases at Statistics Canada

**Prevalence**

The number of people with a new or previous cancer diagnosis in a given population who are alive on a specific date (known as the index date).

## Prevention and control

Important risk factors for HCC are smoking, alcohol-related cirrhosis and fatty liver disease, which means that ongoing efforts should be made to address tobacco use, alcohol abuse and excess body weight. However, large strides in the control of liver cancer will also be achieved by addressing viral hepatitis infection. Currently neither HBV nor HCV infections are well recognized by the public as threats to health, even though they pose the greatest risk for liver cancer.[38] According to the Public Health Agency of Canada, approximately 600,000 Canadians are infected with HBV or HCV.

There is strong evidence that implementing universal vaccination against hepatitis B results in a decrease in HCC.[39] All provinces in Canada now offer universal vaccination against hepatitis B, although the strategies vary from province to province. Some offer universal vaccination to newborns and others to adolescents.[40] All medical bodies that have opinions on hepatitis B vaccination recommend neonatal vaccination. This is because infection in infancy often leads to life-long chronic infection with the virus, whereas infection in adults results in chronic infection in less than 1% of cases. The incidence of childhood hepatitis B is either stable or rising in provinces where adolescent vaccination is offered, but it is falling in British Columbia where neonatal vaccination is offered.[41] In Canada, most cases of HBV infection are in adult immigrants from countries where universal vaccination is either not offered or was introduced only recently.

In the absence of randomized trials, the role that treatment for hepatitis B plays in reducing the incidence of HCC is unclear. Recent studies suggest that treatment with lamivudine can reduce HCC incidence in the presence and absence of cirrhosis.[42–44] Currently, however, only a very small proportion of people with chronic hepatitis B are receiving treatment. This is in part because of the poor recognition of the severity of hepatitis B consequences by infected people and family practitioners and because of the restricted access to hepatitis B antiviral agents through provincial drug reimbursement plans.

One randomized controlled trial showed that screening of people with hepatitis B can reduce HCC-related mortality by 37%.[45] Other studies also strongly suggest that screening reduces HCC-related mortality,[46–49] which supports the recommendation by all major international hepatology associations for the regular screening of HBV-infected people at risk for HCC. Modelling studies also suggest that screening immigrants for hepatitis B is cost effective and will reduce the incidence of complications of hepatitis B.[50]

As with hepatitis B, there is some evidence that treating HCV reduces HCC incidence,[46–49, 51] although the evidence is not strong. Despite low cure rates in the past, HCV treatment today is thought to cure the infection in 65% to 70% of people. However, less than 3% of chronically infected people receive treatment each year. It is estimated that only about 80,000 HCV-positive people in Canada have been treated over the last 15 to 20 years.[52, 53] As with HBV, the limited number of people treated for HCV is due to the lack of awareness among primary care physicians and because of restrictive drug reimbursement policies.

### Population-level initiatives

Governments in many other Western countries (including the US, Australia, France, Germany and New Zealand) have developed concerted strategies to identify and offer treatment to individuals infected with HBV or HCV. For example, in 2008 the US Centers for Disease Control and Prevention (CDC) published updated guidelines for HBV screening, which broadened screening to all individuals in the US who lived in or were born in world regions with intermediate or high HBV prevalence (>2%).[54] Recommendations by the US Institute of Medicine were also updated to reflect expanded community-based programs for HBV screening, testing and vaccination services for immigrants.[55]

More recently, the CDC recommended at least a one-time blood test for HCV for all individuals born in North America between 1945 and 1965.[12] This recommendation is supported by statistical modelling of sequelae and studying the cost-effectiveness of treatment. There is no similar recommendation in Canada, but the Public Health Agency of Canada is examining the issue. In Canada, other options (such as a catch-up immunization program) could be considered for children and young adults from at-risk regions who have not been vaccinated against HBV. Other approaches could include screening and treatment for HBV and HCV in immigrants from high prevalence world regions,[11] public education among at-risk populations to reduce stigma and raise awareness of the prevalence of and testing for hepatitis infection, and greater implementation of safe injection sites and needle exchange programs for drug users.[56]

### Healthcare professional initiatives

Healthcare professionals must also recognize people who would benefit from increased monitoring or screening for risk factors and to whom they should offer treatment. Barriers to effective care may be related to low rates of community surveillance for people with cirrhosis or those at high risk of HCC.[57, 58] These low rates of surveillance may be due to the difficulty in implementing regular surveillance, complicated diagnostic evaluation, limited access to specialized multidisciplinary care and the high cost of potentially curative therapy.[28, 59] Surveillance with liver ultrasound and measurement of serum alpha-fetoprotein levels every 6 to 12 months in people with cirrhosis or advanced hepatic fibrosis, irrespective of the cause, improves diagnosis of HCC at early stages when the tumour might be curable by surgical resection, liver transplantation or RFA. Using these measures to diagnose liver cancer at an early stage also means that a five-year survival higher than 50% can be achieved.[28, 60]

Offering testing and counselling to HIV-positive people would also be beneficial as these individuals are at greater risk of HBV or HCV co-infection due to common risk factors.[61]

### Individual-level initiatives

People may be unaware that they are infected with hepatitis B or C, which can be an impediment to the control of liver cancer.[5] Initiatives to raise awareness about viral hepatitis should consider the heterogeneous nature of the demographic profile, language, cultural perceptions of disease, health literacy and frequency of contact with medical care of the targeted at-risk communities.

Testing for HBV or HCV can mean that treatment is started sooner, which can help clear the virus, lessen the damage to the liver and prevent further spread of the infection to others. Risk reduction involves practising safe sex, not sharing needles or other drug-related equipment, effective sterilizing of tattooing and body piercing equipment and not sharing personal hygiene materials that can come into contact with blood (such as razors and toothbrushes).

## Costs associated with liver cancer care

The increase in HCC incidence creates a greater demand for screening, diagnosis, care and treatment. Representative cost data are needed to create policy decision models. They are designed to explicitly include resource consequences and health outcomes in a health economic evaluation framework to evaluate whether particular healthcare technologies should be provided within the context of an organized healthcare system.

Net costs of care represent the difference between the mean costs for people with HCC compared to people with similar characteristics without HCC.[62] Net costs can be calculated by phase of disease where the initial phase of HCC is defined as the first 12 months after diagnosis and includes diagnostic services and curative treatments.[65] The terminal phase is the final 12 months of life and involves care received at the end of life.[65] The continuing care phase is all months between the initial and terminal phases of care. This care phase includes surveillance activities for detecting recurrences, medications to prevent cancer recurrence and treatment of complications from the initial therapy. For people who survive less than 24 months after diagnosis, the final 12 months of observation and costs of care were allocated first to the terminal phase, consistent with other studies.[63, 64]

Between 1990 and 2009, the estimated average net cost of HCC care per 30 patient-days in Ontario was $7,134 (in 2010 Canadian dollars) in the initial phase of the disease. This cost represents 92% of the total costs of care in this phase (Table 7.5). In the continuing care phase, the cost is $1,159, which represents 58% of the total costs of care in this phase. In the terminal phase, the cost is $10,265, which represents 72% of the total costs of care in this phase.

### Estimates of five-year net costs of HCC care

The mean five-year net costs of HCC care were estimated using an incidence approach that applied phase-specific net costs of care due to HCC to survival probabilities (from the date of diagnosis to death) and by aggregating the costs of the three phases.[63, 66, 67] When undiscounted, the five-year net costs of HCC are estimated to be $126,406 (95% CI, $94,646–$158,166). With a 3% discount, the estimate was $79,516 ($59,934–$99,098), and it was $70,170 ($53,062–$87,278) with a 5% discount.

**Discounting**

The process of converting future values (e.g., costs or health effects) to their present values to reflect the fact that individuals and society generally prefer to receive benefits sooner rather than later and pay costs later rather than sooner.

### Aggregate five-year net costs of HCC care in the Canadian population

When the mean five-year net costs were applied to the newly diagnosed cases of HCC in the Canadian population in 2009, the five-year aggregate net costs of care were approximately $174 million (95% CI, $130 million–$217 million) when undiscounted. With a 3% discount the five-year aggregate net costs of care were $109 million ($82 million–$136 million) and they were $96 million ($73 million–$120 million) with a 5% discount.

## New developments in liver cancer management and research

### Treatments

Based on available evidence[42,43,49,68,69], eradicating hepatitis C and controlling hepatitis B replication appear to be associated with a lower risk for and less disease progression of HCC. However, there are currently no randomized controlled trials that convincingly show how treating viral hepatitis affects liver cancer mortality. The biggest limitation to treating HCC is the function of the underlying liver. Unless liver function is normal (or near normal), none of the usual treatments are possible. People with Child-Pugh class B cirrhosis are not candidates for any form of therapy.[26] These limitations extend to all the newer therapies currently being developed. The most recent development in the management of HCC is the introduction of sorafenib,[70] the first agent to be licensed for the treatment of HCC. The introduction of this drug has led to investigations into other agents, including brivanib, sunitinib, tivantinib and regorafenib. Tivantinib and regorafenib are still under investigation, while brivanib and sunitinib have failed phase III trials and are no longer being developed for HCC. The success of sorafenib in treating advanced disease also prompted investigation of its utility in earlier stage disease. While these studies are not yet complete, it is thought that sorafenib does not enhance the effect of chemoembolization.

Standard chemotherapy has not been shown to be effective in treating HCC, in part due to the severity of the underlying liver disease. People with advanced liver disease do not tolerate chemotherapy well. The experimental approaches include different methods to deliver therapeutic agents to the tumour. The most advanced of these approaches is radio-embolization, which has shown impressive tumour necrosis.[71, 72] To date there are no direct comparisons between radio-embolization and other treatments applied to the same person with HCC. However, studies comparing survival of people treated with radio-embolization to people not treated by this method suggest an improvement in survival.[73]

Another experimental approach to delivering local chemotherapy involves the use of biodegradable microspheres loaded with a chemotherapeutic agent.[74] Compared to standard chemoembolization, this approach appears to be safer, but it does not appear to improve survival. Other researchers have combined RFA with local chemotherapy. This technique is still under investigation.

Traditionally, radiation therapy has not been used for HCC because of concerns that the liver was radiosensitive. However, researchers are currently studying a number of techniques using external beam radiation therapy, such as intensity-modulated radiation therapy (IMRT), image-guided radiation therapy, 3-dimensional conformal radiation, 4-dimensional conformal radiation and charged particle therapy.[75–77]

### Genetic studies

As with other cancers, researchers have attempted to identify pathways that lead to the development of HCC, but so far they have not identified a "driver" genetic alteration. However, researchers have identified different sets of genes that are over- or under-expressed in HCC. Although there has been some attempt to classify these diverse results into four main genotypes,[78] many HCCs do not fit into this classification method.

Researchers have identified gene signatures that predict better or worse prognosis for HCC,[79–81] but to date they have not identified gene expression that can be used as a target for drug intervention. Most notable is the finding that a gene signature in the healthy portion of liver that is removed with the tumour during surgery predicts recurrence two years or more after surgery.[82] This finding suggests that the whole liver or large parts of it consist of a clonal population of cells, which means that it may be possible to biopsy a liver without cancer in a person at risk for HCC and predict whether it will or will not develop HCC.

## What do these statistics mean?

The burden of liver cancer in Canada is expected to grow as a result of an aging population and the ongoing trend in immigration from countries where HBV and HCV infections are endemic. The control of HCV infection continues to pose a challenge in Canada, particularly in marginalized populations.

Researchers have shown that screening for HCC can increase the chance of being successfully treated for this cancer. Yet most people with HCC have not undergone proper screening and it appears that the vast majority of at-risk people are not undergoing screening. All people at risk for HCC should be made aware of their need for screening and healthcare providers need to be educated about who to screen and which tests to use.

Greater efforts are needed to prevent liver cancer. These efforts should include public and healthcare provider education, early identification of individuals at risk of the disease, increasing the use of hepatitis screening among at-risk individuals and policies to facilitate treatment of people with liver cancer. Control of more widespread risk factors, such as smoking, alcohol abuse and excess weight, can help reduce incidence of liver and other cancers.
Recommendations to improve the control of liver cancer in Canada include:

- Healthcare providers should identify, offer testing to and counsel people at risk for liver cancer based on their hepatitis, alcohol, weight and diabetes profiles. Healthcare providers should aim to identify people early in the course of chronic HBV or HCV infection. They should also offer testing and counselling for HIV-positive people because they are at greater risk of HBV or HCV co-infection due to common risk factors.
- Canadians need easier access to HBV and HCV treatments to reduce the chance of progression to liver cancer.
- Public health messages should aim to raise the profile of this rapidly rising disease and emphasize the ways to prevent it. Public health efforts should not be limited to clinic visits; outreach should be done to increase risk-reduction education, provide support for people with HCC and offer catch-up HBV vaccination. Education on risk reduction for HCC should encompass not only testing for and treating viral hepatitis, but also the impact of alcohol abuse, obesity and smoking.
- More Canadian data are needed to understand the best strategies for HBV and HCV screening and treatment, as well as the best ways to improve community engagement in promoting screening for populations that are hard to reach.
- The approaches to HBV and HCV testing strategies undertaken in other countries should be considered for the Canadian context.
- The higher risk of the disease in lower income populations and barriers to access to healthcare, early detection and treatment need to be investigated further to reduce the impact on this population.

As liver cancer incidence increases, access to potentially curative therapies and the costs associated with them will present new challenges to the healthcare system. Further research is needed to find the most effective means of educating the public about the disease, screening for people at risk for HBV and HCV infection and understanding the needs of people with and survivors of liver cancer. In addition, current and future interventions can benefit from an understanding of their cost-effectiveness, barriers to implementation and impact on future rates of the disease.

## For further information

### Publications

- Kachuri L, De P, Ellison LF, Semenciw R. Cancer incidence, mortality and survival trends in Canada, 1970–2007. *Chronic Diseases and Injuries in Canada*. 2013;33(2):69–80.
- Jiang X, Pan SY, de Groh M, Liu S, Morrison H. Increasing incidence in liver cancer in Canada, 1972–2006: Age-period-cohort analysis. *Journal of Gastrointestinal Oncology*. 2011;2(4):223–31.
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- elSaadany S, Tepper M, Mao Y, Semenciw R, Giulivi A. An epidemiologic study of hepatocellular carcinoma in Canada. *Canadian Journal of Public Health*. 2002;93(6):443–6.

### Databases

- Statistics Canada. Table 103-0550 — New cases for ICD-O-3 primary sites of cancer (based on the July 2011 CCR tabulation file), by age group and sex, Canada, provinces and territories, annual, CANSIM (database).
- Statistics Canada. Table 103-0553 — New cases and age-standardized rate for ICD-O-3 primary sites of cancer (based on the July 2011 CCR tabulation file), by sex, Canada, provinces and territories, annual, CANSIM (database).
- Statistics Canada. Table 102-0552 — Deaths and mortality rate, by selected grouped causes and sex, Canada, provinces and territories, annual, CANSIM (database).
- Statistics Canada. Table 102-4309 — Mortality and potential years of life lost, by selected causes of death and sex, three-year average, Canada, provinces, territories, health regions and peer groups, occasional (number unless otherwise noted), CANSIM (database).
- Statistics Canada. Table 103-1574 — Five-year survival estimates for primary sites of cancer, ICD-O-3 (October 2011 CCR file), by sex, population aged 15 to 99, 3 years of cases, selected provinces, annual (percent), 1992/1994 to 2001/2003, CANSIM (database).
- Statistics Canada. Table 103-1572 — Age-standardized five-year survival estimates for primary sites of cancer, ICD-O-3 (October 2011 CCR file), by sex, 3 years of cases, Canada and selected provinces, annual (percent), 1992/1994 to 2001/2003, CANSIM (database).
- Public Health Agency of Canada. Chronic Disease Infobase Cubes. Ottawa, Canada.

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**TABLE 7.1** New cases and percent distribution for liver cancer by morphology, Canada*, 1992–2010

| | Total | | Males | | Females | |
|---|---|---|---|---|---|---|
| | New cases | % | New cases | % | New cases | % |
| **All liver cancers** | **20,368** | **100** | **15,063** | **100** | **5,305** | **100** |
| **Morphology** | | | | | | |
| Carcinoma | 16,354 | 80.3 | 12,358 | 82.0 | 3,996 | 75.3 |
| Hepatocellular carcinoma (HCC) | 14,650 | 71.9 | 11,328 | 75.2 | 3,322 | 62.6 |
| Cholangiocarcinoma | 833 | 4.1 | 479 | 3.2 | 354 | 6.7 |
| Other specific carcinoma | 347 | 1.7 | 221 | 1.5 | 126 | 2.4 |
| Unspecified, carcinoma | 524 | 2.6 | 330 | 2.2 | 194 | 3.7 |
| Hepatoblastoma | 220 | 1.1 | 132 | 0.9 | 88 | 1.7 |
| Sarcoma | 136 | 0.7 | 84 | 0.6 | 52 | 1.0 |
| Other specific types | 31 | 0.2 | 17 | 0.1 | 14 | 0.3 |
| Unspecified | 3,627 | 17.8 | 2,472 | 16.4 | 1,155 | 21.8 |

**Analysis by:** Chronic Disease Surveillance and Monitoring Division, CCDP, Public Health Agency of Canada
**Data source:** Canadian Cancer Registry database at Statistics Canada

* Actual incidence data were available up to 2010 for all provinces and territories except for Quebec (2007).

**TABLE 7.2** HCC treatment strategies by stage* of disease

| Stage | Definition | Option |
|---|---|---|
| **Very early** | Single, asymptomatic lesion measuring less than 2 cm in diameter, with no vascular or distant metastases | • Local ablation with radiofrequency ablation (RFA) or resection[27, 83]<br>• Resection can only be offered to people with no or minimal evidence of liver failure or of portal hypertension.<br>• RFA can be offered to people with more advanced liver disease, but those with the most advanced liver disease can only benefit from liver transplantation,[84] but then only if the cancer is at an early stage. |
| **Early** | Single lesion or fewer than 3 lesions (each smaller than 3 cm) | • Resection, liver function allowing<br>• People with early stage disease are also candidates for liver transplantation.[85]<br>• Chemoembolization has also been offered to people with early stage disease, but the benefit of chemoembolization in these people has not yet been demonstrated. |
| **Intermediate** | Multinodular disease (either >3 nodules or 2–3 nodules with at least 1 nodule >5 cm) | • Chemoembolization[86, 87] |
| **Advanced** | Spread beyond the liver to local nodes or distant sites, or invasion of portal vein or hepatic vein by tumour | • Sorafenib, an oral multikinase inhibitor[70, 88]<br>• The role of transarterial chemoembolization (TACE) remains to be defined. |

HCC=hepatocellular carcinoma

* Based on the Barcelona Clinic Liver Cancer (BCLC) staging system.[26]

**TABLE 7.3** Five-year relative survival ratios (RSRs) for primary liver cancer by sex and age group, Canada (excluding Quebec*), 2006–2008

| | Both sexes | | Males | | Females | |
|---|---|---|---|---|---|---|
| | RSR (%) | (95% CI) | RSR (%) | (95% CI) | RSR (%) | (95% CI) |
| All ages (15–99 years) | 20 | (18–22) | 20 | (18–22) | 19 | (16–22) |
| 15–49 | 38 | (32–43) | 34 | (27–40) | 46 | (32–58) |
| 50–59 | 23 | (20–26) | 22 | (19–25) | 28 | (20–36) |
| 60–69 | 22 | (18–25) | 22 | (18–26) | 21 | (15–28) |
| 70–79 | 15 | (12–18) | 16 | (12–19) | 12 | (7–18) |
| 80–99 | 7 | (4–11) | 6 | (3–11) | 7 | (3–13) |

CI=confidence interval

* Data from Quebec were excluded, in part, because the method for ascertaining the date of cancer diagnosis differs from the method used by other provinces and territories and because of issues in correctly ascertaining the vital status of cases.

**Analysis by:** Health Statistics Division, Statistics Canada
**Data sources:** Canadian Cancer Registry and Canadian Vital Statistics Death databases and life tables at Statistics Canada

**TABLE 7.4** Observed survival of people diagnosed with HCC, by income quintile and treatment, Ontario, 1990–2009

| | Cases | Events | Survival (months) | 1-year survival | 2-year survival | 5-year survival |
|---|---|---|---|---|---|---|
| Characteristics | N (%) | N | Median (95 % CI) | (%) (95% CI) | (%) (95% CI) | (%) (95% CI) |
| Overall | 5,481 (100) | 4,181 | 9.2 (8.7–10.0) | 45.2 (43.9–46.6) | 29.8 (28.5–31.2) | 13.2 (12.0–14.3) |
| Income quintile | | | | | | |
| 1 (lowest) | 1,323 (24.1) | 1,024 | 8.5 (7.3–9.9) | 43.5 (40.7–46.3) | 29.0 (26.3–31.7) | 11.9 (9.7–14.1) |
| 2 | 1,196 (21.8) | 905 | 8.9 (7.9–11.1) | 44.9 (42.0–47.9) | 29.4 (26.5–32.2) | 12.6 (10.2–14.9) |
| 3 | 1,030 (18.8) | 776 | 10.5 (8.8–12.2) | 47.2 (44.0–50.4) | 31.1 (28.0–34.2) | 13.8 (11.2–16.5) |
| 4 | 915 (16.7) | 692 | 10.4 (9.1–12.2) | 46.7 (43.3–50.1) | 30.6 (27.3–33.9) | 12.9 (10.1–15.7) |
| 5 (highest) | 893 (16.3) | 667 | 8.8 (7.8–10.6) | 45.4 (42.0–48.8) | 30.9 (27.6–34.2) | 15.3 (12.3–18.2) |
| HCC treatment* | | | | | | |
| Curative | 1,637 (29.9) | 766 | 44.4 (40.4–46.9) | 82.1 (80.1–84.1) | 68.1 (65.5–70.7) | 40.4 (37.2–43.6) |
| Non-curative | 890 (16.2) | 627 | 21.4 (19.1–23.0) | 65.6 (62.4–68.9) | 45.1 (41.5–48.6) | 19.9 (16.8–23.2) |
| Palliative | 1,906 (34.8) | 1,755 | 8.8 (8.1–9.7) | 42.7 (40.4–45.0) | 24.3 (22.3–26.3) | 7.8 (6.5–9.1) |
| No treatment | 2,034 (37.1) | 1,765 | 4.2 (3.7–4.6) | 27.6 (25.6–29.6) | 15.4 (13.7–17.1) | 3.7 (2.7–4.7) |

HCC=hepatocellular carcinoma; CI=confidence interval

* Included multiple treatments for some people.

**Adapted from:** Jembere N, et al.[35]

**TABLE 7.5** Mean net costs* of care for HCC (per 30 patient-days) by cost category and disease phase, Ontario, 1990–2009

| Cost category | Disease phase | | | | | |
|---|---|---|---|---|---|---|
| | Initial | | Continuing care | | Terminal | |
| | Mean | (95% CI) | Mean | (95% CI) | Mean | (95% CI) |
| Total net costs | 7,134 | (5,644, 8,623) | 1,159 | (942, 1,376) | 10,265 | (7,990, 12,540) |
| Outpatient visits | 3,815 | (2,960, 4,670) | 422 | (306, 538) | 2,927 | (1,687, 4,167) |
| Emergency room visits | 150 | (96, 203) | 43 | (15, 71) | 430 | (269, 590) |
| Same-day surgery | 59 | (19, 99) | 4 | (–2, 10) | 36 | (17, 54) |
| Acute inpatient care | 2,734 | (1,990, 3,478) | 332 | (245, 419) | 6,725 | (5,597, 7,853) |
| Medications | 232 | (125, 339) | 294 | (240, 349) | 67 | (37, 97) |
| Home care | 139 | (93, 184) | 93 | (17, 169) | 294 | (215, 374) |
| Continuing care | 19 | (–26 ,63) | 3 | (–32, 39) | 208 | (–197, 613) |
| Long-term care | –24 | (–40, –7) | –42 | (–67, –17) | –420 | (–486, –355) |

HCC=hepatocellular carcinoma; CI=confidence interval

*2010 Canadian dollars

**Note:** Categories are assigned as initial phase (12 months after the diagnosis), continuing care phase (intermediate observation time) and terminal phase (12 months prior to death). Negative costs refer to no increase in the net costs of long-term care due to HCC. Columns may not add to total.

**Analysis based on:** Thein HH, et al.[89]

# APPENDIX I: Actual data for new cases and deaths

**TABLE A1** Actual data for new cases of cancer, Canada, 2007 (based on September 2012 CCR file; see Statistics Canada CANSIM Table 103-0553 for availability of later data releases)

| Cancer | ICD-O-3 Site/Type* | Total | Males | Females |
|---|---|---|---|---|
| **All cancers** | **All invasive sites** | **164,999** | **86,198** | **78,801** |
| **Oral (buccal cavity and pharynx)** | **C00–C14** | **3,675** | **2,497** | **1,178** |
| Lip | C00 | 338 | 254 | 84 |
| Tongue | C01–C02 | 936 | 648 | 288 |
| Salivary gland | C07–C08 | 419 | 230 | 189 |
| Mouth | C03–C06 | 712 | 402 | 310 |
| Nasopharynx | C11 | 259 | 183 | 76 |
| Oropharynx | C10 | 165 | 116 | 49 |
| Other and unspecified | C09,C12–C14 | 846 | 664 | 182 |
| **Digestive organs** | **C15–C26,C48** | **34,144** | **19,121** | **15,023** |
| Esophagus | C15 | 1,585 | 1,194 | 391 |
| Stomach | C16 | 3,076 | 1,960 | 1,116 |
| Small intestine | C17 | 614 | 341 | 273 |
| Large intestine | C18,C26.0 | 13,865 | 7,112 | 6,753 |
| Rectum | C19–C20 | 6,763 | 4,147 | 2,616 |
| Anus | C21 | 558 | 231 | 327 |
| Liver | C22.0 | 1,610 | 1,217 | 393 |
| Gallbladder | C23 | 463 | 152 | 311 |
| Pancreas | C25 | 3,979 | 1,989 | 1,990 |
| Other and unspecified | C22.1,C24,C26.8–.9,C48 | 1,631 | 778 | 853 |
| **Respiratory system** | **C30–C34,C38.1–.9,C39** | **24,714** | **13,792** | **10,922** |
| Larynx | C32 | 1,116 | 906 | 210 |
| Lung | C34 | 23,246 | 12,677 | 10,569 |
| Other and unspecified | C30–31,C33,C38.1–.9,C39 | 352 | 209 | 143 |
| **Bone** | **C40–C41** | **349** | **195** | **154** |
| **Soft tissue (including heart)** | **C38.0,C47,C49** | **1,118** | **619** | **499** |
| **Skin (melanoma)** | **C44 Type 8720–8790** | **4,843** | **2,565** | **2,278** |
| **Breast** | **C50** | **21,311** | **165** | **21,146** |
| **Genital organs** | **C51–C63** | **33,567** | **24,382** | **9,185** |
| Cervix | C53 | 1,405 | — | 1,405 |
| Body of uterus | C54 | 4,369 | — | 4,369 |
| Uterus, part unspecified | C55 | 150 | — | 150 |
| Ovary | C56 | 2,463 | — | 2,463 |
| Prostate | C61 | 23,364 | 23,364 | — |
| Testis | C62 | 828 | 828 | — |
| Other and unspecified | C51–52,C57,C58,C60,C63 | 988 | 190 | 798 |
| **Urinary organs** | **C64–C68** | **12,055** | **8,152** | **3,903** |
| Bladder | C67 | 6,744 | 4,939 | 1,805 |
| Kidney | C64–C65 | 4,837 | 2,883 | 1,954 |
| Other urinary | C66,C68 | 474 | 330 | 144 |
| **Eye** | **C69** | **290** | **161** | **129** |
| **Brain and central nervous system** | **C70–C72** | **2,591** | **1,468** | **1,123** |
| **Endocrine glands** | **C37,C73–C75** | **4,462** | **1,069** | **3,393** |
| Thyroid | C73 | 4,181 | 944 | 3,237 |
| Other endocrine | C37,C74–C75 | 281 | 125 | 156 |
| **Hodgkin lymphoma†** | **Type 9650–9667** | **922** | **505** | **417** |
| **Non-Hodgkin lymphoma†** | **See Table A7** | **6,789** | **3,770** | **3,019** |
| **Multiple myeloma†** | **Type 9731,9732,9734** | **2,011** | **1,081** | **930** |
| **Leukemia†** | **See Table A7** | **4,848** | **2,784** | **2,064** |
| **Mesothelioma†** | **Type 9050–9055** | **515** | **420** | **95** |
| **All other and unspecified cancers** | **See Table A7** | **6,795** | **3,452** | **3,343** |

**Analysis by:** Chronic Disease Surveillance and Monitoring Division, CCDP, Public Health Agency of Canada
**Data source:** Canadian Cancer Registry database at Statistics Canada

— Not applicable.

* Fritz A, Percy C, Jack A, Shanmugaratnam K, Sobin L, Parkin D, et al. Editors. *International Classification of Diseases for Oncology, Third Edition*. Geneva: World Health Organization; 2000.

† ICD-O-3 histology types 9590–9992 (leukemia, lymphoma and multiple myeloma), 9050–9055 (mesothelioma) and 9140 (Kaposi sarcoma) are excluded from other specific organ sites.

**Note:** Numbers are for invasive cancers and *in situ* bladder cancers (except for Ontario) but exclude non-melanoma skin cancer (basal and squamous).

**TABLE A2** Actual data for cancer deaths, Canada, 2009 (see Statistics Canada CANSIM Table 102-0552 for availability of later data releases)

| | ICD-10* | Total | Males | Females |
|---|---|---|---|---|
| **All cancers** | **C00–C97** | **71,125** | **37,452** | **33,673** |
| **Oral (buccal cavity and pharynx)** | **C00–C14** | **1,065** | **721** | **344** |
| Lip | C00 | 17 | 9 | 8 |
| Tongue | C01–C02 | 259 | 169 | 90 |
| Salivary gland | C07–C08 | 107 | 68 | 39 |
| Mouth | C03–C06 | 173 | 97 | 76 |
| Nasopharynx | C11 | 92 | 58 | 34 |
| Oropharynx | C10 | 104 | 80 | 24 |
| Other and unspecified | C09,C12–C14 | 313 | 240 | 73 |
| **Digestive organs** | **C15–C25,C26.0,C26.8–.9,C48** | **19,115** | **10,704** | **8,411** |
| Esophagus | C15 | 1,685 | 1,264 | 421 |
| Stomach | C16 | 1,911 | 1,177 | 734 |
| Small intestine | C17 | 175 | 92 | 83 |
| Large intestine | C18,C26.0 | 6,599 | 3,422 | 3,177 |
| Rectum | C19–C20 | 2,008 | 1,175 | 833 |
| Anus | C21 | 89 | 38 | 51 |
| Liver | C22.0,C22.2–.7 | 841 | 647 | 194 |
| Gallbladder | C23 | 238 | 75 | 163 |
| Pancreas | C25 | 3,981 | 1,985 | 1,996 |
| Other and unspecified | C22.1,C22.9,C24,C26.8–.9,C48 | 1,677 | 867 | 810 |
| **Respiratory system** | **C30–C34,C38.1–.9,C39** | **19,670** | **11,016** | **8,654** |
| Larynx | C32 | 439 | 368 | 71 |
| Lung | C34 | 19,106 | 10,567 | 8,539 |
| Other and unspecified | C30–31,C33,C38.1–.9,C39 | 125 | 81 | 44 |
| **Bone** | **C40–C41** | **147** | **80** | **67** |
| **Soft tissue (including heart)** | **C38.0,C47,C49** | **471** | **228** | **243** |
| **Skin (melanoma)** | **C43** | **1,019** | **634** | **385** |
| **Breast** | **C50** | **4,990** | **46** | **4,944** |
| **Genital organs** | **C51–C63** | **6,873** | **3,803** | **3,070** |
| Cervix | C53 | 370 | — | 370 |
| Body of uterus | C54 | 504 | — | 504 |
| Uterus, part unspecified | C55 | 358 | — | 358 |
| Ovary | C56 | 1,597 | — | 1,597 |
| Prostate | C61 | 3,745 | 3,745 | — |
| Testis | C62 | 29 | 29 | — |
| Other and unspecified | C51–52,C57,C58,C60,C63 | 270 | 29 | 241 |
| **Urinary organs** | **C64–C68** | **3,633** | **2,409** | **1,224** |
| Bladder | C67 | 1,910 | 1,330 | 580 |
| Kidney | C64–C65 | 1,547 | 974 | 573 |
| Other urinary | C66,C68 | 176 | 105 | 71 |
| **Eye** | **C69** | **30** | **14** | **16** |
| **Brain and central nervous system** | **C70–C72** | **1,867** | **1,102** | **765** |
| **Endocrine glands** | **C37,C73–C75** | **306** | **146** | **160** |
| Thyroid | C73 | 182 | 86 | 96 |
| Other endocrine | C37,C74–C75 | 124 | 60 | 64 |
| **Hodgkin lymphoma** | **C81** | **126** | **71** | **55** |
| **Non-Hodgkin lymphoma** | **C82–C85,C96.3** | **2,597** | **1,419** | **1,178** |
| **Multiple myeloma** | **C90.0, C90.2** | **1,289** | **699** | **590** |
| **Leukemia** | **C91–C95, C90.1** | **2,473** | **1,394** | **1,079** |
| **Mesothelioma** | **C45** | **421** | **355** | **66** |
| **All other and unspecified cancers** | **See Table A7** | **5,033** | **2,611** | **2,422** |

**Analysis by:** Chronic Disease Surveillance and Monitoring Division, CCDP, Public Health Agency of Canada
**Data source:** Canadian Vital Statistics Death database at Statistics Canada

— Not applicable.

*World Health Organization. *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision*. Volumes 1 to 3. Geneva, Switzerland: World Health Organization; 1992.

**TABLE A3** Actual data for new cases for the most common cancers by sex and geographic region, Canada, most recent year* (based on September 2012 CCR file; see Statistics Canada CANSIM Table 103-0553 for availability of later data releases)

| | New cases | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Canada† | BC | AB | SK | MB | ON | QC‡ | NB | NS | PE | NL‡ | YT | NT | NU |
| **Males** | | | | | | | | | | | | | | |
| **All cancers** | **86,200** | **11,000** | **7,700** | **2,500** | **3,000** | **33,700** | **21,400** | **2,400** | **2,900** | **420** | **1,650** | **50** | **60** | **25** |
| Prostate | 23,400 | 2,900 | 2,100 | 610 | 730 | 9,300 | 4,300 | 670 | 720 | 130 | 480 | 15 | 15 | — |
| Lung | 12,700 | 1,350 | 910 | 350 | 390 | 4,400 | 4,100 | 370 | 430 | 75 | 220 | 5 | 10 | 10 |
| Colorectal | 11,300 | 1,400 | 1,000 | 360 | 450 | 4,000 | 2,900 | 300 | 440 | 55 | 280 | 10 | 10 | 5 |
| Bladder§ | 4,900 | 760 | 500 | 190 | 190 | 1,550 | 1,650 | 180 | 210 | 15 | 100 | 5 | — | — |
| Non-Hodgkin lymphoma | 3,800 | 550 | 330 | 130 | 130 | 1,500 | 860 | 95 | 140 | 15 | 60 | — | — | — |
| Kidney | 2,900 | 280 | 260 | 95 | 150 | 1,150 | 730 | 120 | 110 | 20 | 75 | — | — | — |
| Leukemia | 2,800 | 350 | 300 | 100 | 120 | 1,200 | 630 | 90 | 55 | 10 | 35 | — | — | — |
| Melanoma | 2,600 | 430 | 270 | 60 | 90 | 1,400 | 350 | 65 | 130 | 25 | 45 | — | — | — |
| Oral | 2,500 | 370 | 250 | 80 | 110 | 1,050 | 610 | 50 | 75 | 10 | 35 | 5 | 5 | — |
| Pancreas | 2,000 | 240 | 180 | 50 | 90 | 680 | 540 | 40 | 60 | 10 | 20 | — | — | — |
| Stomach | 1,950 | 220 | 160 | 60 | 70 | 710 | 480 | 50 | 55 | 10 | 65 | — | — | — |
| Brain | 1,450 | 190 | 120 | 35 | 40 | 570 | 390 | 30 | 55 | 5 | 30 | — | — | — |
| Liver | 1,200 | 200 | 110 | 20 | 30 | 510 | 330 | 15 | 30 | — | 15 | — | — | — |
| Esophagus | 1,200 | 180 | 120 | 40 | 45 | 560 | 280 | 40 | 55 | 5 | 15 | — | — | — |
| Multiple myeloma | 1,100 | 180 | 110 | 40 | 40 | 520 | 280 | 30 | 35 | 5 | 20 | — | — | — |
| Thyroid | 940 | 100 | 100 | 20 | 30 | 490 | 200 | 30 | 30 | 5 | 20 | — | — | — |
| **Females** | | | | | | | | | | | | | | |
| **All cancers** | **78,800** | **10,200** | **7,000** | **2,400** | **3,000** | **33,000** | **20,500** | **1,950** | **2,700** | **380** | **1,300** | **55** | **55** | **25** |
| Breast | 21,100 | 3,000 | 2,100 | 650 | 790 | 8,900 | 5,400 | 530 | 720 | 120 | 340 | 15 | 20 | 5 |
| Lung | 10,600 | 1,300 | 870 | 350 | 420 | 3,900 | 3,100 | 270 | 420 | 50 | 150 | 10 | 5 | 10 |
| Colorectal | 9,400 | 1,150 | 770 | 340 | 400 | 3,600 | 2,500 | 250 | 380 | 40 | 210 | 5 | 10 | 5 |
| Body of uterus | 4,500 | 670 | 440 | 150 | 220 | 2,100 | 1,100 | 130 | 160 | 15 | 100 | 5 | — | — |
| Thyroid | 3,200 | 240 | 320 | 60 | 90 | 2,000 | 740 | 95 | 85 | 10 | 45 | — | — | — |
| Non-Hodgkin lymphoma | 3,000 | 430 | 290 | 100 | 130 | 1,300 | 720 | 75 | 95 | 15 | 60 | — | — | — |
| Ovary | 2,500 | 280 | 170 | 65 | 90 | 1,050 | 650 | 55 | 70 | 15 | 35 | — | — | — |
| Melanoma | 2,300 | 390 | 230 | 70 | 75 | 1,150 | 270 | 55 | 120 | 10 | 25 | — | — | — |
| Leukemia | 2,100 | 250 | 190 | 70 | 75 | 960 | 450 | 55 | 45 | 5 | 10 | — | — | — |
| Pancreas | 2,000 | 220 | 150 | 65 | 80 | 760 | 560 | 55 | 60 | 10 | 25 | — | — | — |
| Kidney | 1,950 | 140 | 160 | 65 | 70 | 700 | 490 | 55 | 85 | 10 | 40 | — | — | — |
| Bladder§ | 1,800 | 210 | 150 | 65 | 60 | 510 | 630 | 60 | 75 | 10 | 35 | — | — | — |
| Cervix | 1,400 | 180 | 150 | 45 | 40 | 580 | 300 | 25 | 35 | 5 | 40 | — | — | — |
| Oral | 1,200 | 150 | 100 | 30 | 60 | 490 | 270 | 25 | 45 | 5 | 15 | — | — | — |
| Brain | 1,100 | 120 | 80 | 25 | 35 | 480 | 310 | 15 | 30 | 5 | 20 | — | — | — |
| Stomach | 1,100 | 130 | 85 | 30 | 40 | 460 | 300 | 20 | 25 | — | 20 | — | — | — |
| Multiple myeloma | 930 | 140 | 75 | 35 | 35 | 420 | 220 | 25 | 30 | 5 | 20 | — | — | — |

— Fewer than 3 cases per year.

* 2007 for Canada, Quebec; 2010 for British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador; 2006–2010 average for Yukon, Northwest Territories, Nunavut. The numbers of cases from death certificate only for Ontario and Newfoundland and Labrador in 2008–2010 are estimated.

† Row totals may not equal the total for Canada due to rounding and difference in the most recent year of data presented. Canada totals include provincial and territorial estimates.

‡ The number of cases for some cancers used to calculate the overall 2013 estimates for this province was underestimated.

§ Ontario does not report *in situ* bladder cases. If Ontario *in situ* cases were included, it is estimated that the total number of Ontario bladder cancers would be 2,400 among men and 830 among women.

**Note:** "All cancers" excludes the estimated new cases of non-melanoma skin cancer (basal and squamous).

**Analysis by:** Chronic Disease Surveillance and Monitoring Division, CCDP, Public Health Agency of Canada
**Data source:** Canadian Cancer Registry database at Statistics Canada

**TABLE A4** Actual age-standardized incidence rates (ASIR) for the most common cancers by sex and geographic region, Canada, most recent year*
(based on September 2012 CCR file; see Statistics Canada CANSIM Table 103-0553 for availability of later data releases)

| | Cases per 100,000 | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Canada† | BC | AB | SK | MB | ON | QC‡ | NB | NS | PE | NL‡ | YT | NT | NU |
| **Males** | | | | | | | | | | | | | | |
| **All cancers** | **467** | **386** | **417** | **406** | **435** | **441** | **479** | **477** | **471** | **455** | **493** | **330** | **403** | **382** |
| Prostate | 126 | 102 | 112 | 97 | 105 | 121 | 95 | 130 | 113 | 131 | 135 | 92 | 97 | — |
| Lung | 69 | 47 | 52 | 56 | 57 | 57 | 92 | 74 | 69 | 82 | 65 | 46 | 67 | 170 |
| Colorectal | 61 | 49 | 56 | 58 | 63 | 52 | 65 | 59 | 71 | 56 | 83 | 46 | 80 | 60 |
| Bladder§ | 27 | 26 | 28 | 30 | 27 | 21 | 37 | 36 | 34 | 17 | 30 | 25 | — | — |
| Non-Hodgkin lymphoma | 20 | 19 | 18 | 22 | 19 | 20 | 19 | 20 | 22 | 17 | 19 | — | — | — |
| Leukemia | 16 | 13 | 17 | 17 | 17 | 16 | 15 | 19 | 9 | 8 | 12 | — | — | — |
| Kidney | 15 | 10 | 13 | 16 | 20 | 15 | 16 | 24 | 18 | 21 | 21 | — | — | — |
| Melanoma | 14 | 15 | 14 | 10 | 12 | 18 | 8 | 13 | 22 | 29 | 13 | — | — | — |
| Oral | 13 | 12 | 12 | 12 | 15 | 13 | 13 | 10 | 11 | 9 | 11 | 11 | 23 | — |
| Pancreas | 11 | 8 | 10 | 8 | 12 | 9 | 12 | 7 | 9 | 9 | 6 | — | — | — |
| Stomach | 11 | 8 | 9 | 10 | 9 | 9 | 11 | 10 | 9 | 13 | 21 | — | — | — |
| Brain | 8 | 7 | 6 | 7 | 6 | 8 | 9 | 6 | 10 | 5 | 10 | — | — | — |
| Esophagus | 6 | 6 | 6 | 7 | 6 | 7 | 6 | 7 | 9 | 5 | 4 | — | — | — |
| Liver | 6 | 7 | 6 | 4 | 4 | 7 | 7 | 3 | 5 | — | 4 | — | — | — |
| Multiple myeloma | 6 | 6 | 6 | 6 | 6 | 7 | 6 | 6 | 6 | 3 | 5 | — | — | — |
| Thyroid | 5 | 4 | 5 | 4 | 5 | 7 | 4 | 7 | 5 | 7 | 6 | — | — | — |
| **Females** | | | | | | | | | | | | | | |
| **All cancers** | **365** | **324** | **342** | **348** | **369** | **376** | **377** | **351** | **386** | **364** | **360** | **335** | **386** | **375** |
| Breast | 99 | 98 | 100 | 95 | 100 | 103 | 102 | 96 | 103 | 115 | 90 | 91 | 96 | 53 |
| Lung | 48 | 40 | 44 | 48 | 50 | 43 | 56 | 45 | 56 | 45 | 38 | 65 | 60 | 152 |
| Colorectal | 41 | 33 | 37 | 45 | 45 | 38 | 43 | 42 | 50 | 38 | 55 | 45 | 89 | 76 |
| Body of uterus | 21 | 21 | 21 | 22 | 27 | 24 | 20 | 22 | 22 | 15 | 29 | 22 | — | — |
| Thyroid | 18 | 9 | 16 | 11 | 14 | 27 | 17 | 20 | 15 | 11 | 17 | — | — | — |
| Non-Hodgkin lymphoma | 14 | 14 | 14 | 15 | 16 | 15 | 13 | 13 | 13 | 15 | 16 | — | — | — |
| Ovary | 11 | 9 | 8 | 10 | 12 | 12 | 12 | 10 | 9 | 13 | 9 | — | — | — |
| Melanoma | 11 | 14 | 11 | 11 | 10 | 14 | 6 | 10 | 19 | 13 | 7 | — | — | — |
| Leukemia | 10 | 8 | 9 | 10 | 9 | 11 | 9 | 12 | 6 | 8 | 3 | — | — | — |
| Kidney | 9 | 5 | 8 | 9 | 8 | 8 | 9 | 9 | 11 | 8 | 11 | — | — | — |
| Pancreas | 8 | 7 | 7 | 8 | 9 | 8 | 10 | 9 | 8 | 9 | 6 | — | — | — |
| Bladder§ | 8 | 6 | 7 | 9 | 7 | 5 | 11 | 10 | 10 | 6 | 8 | — | — | — |
| Cervix | 8 | 7 | 8 | 8 | 6 | 8 | 7 | 7 | 6 | 9 | 15 | — | — | — |
| Brain | 6 | 4 | 4 | 3 | 5 | 6 | 6 | 3 | 4 | 4 | 6 | — | — | — |
| Oral | 5 | 5 | 5 | 4 | 7 | 6 | 5 | 5 | 6 | 7 | 3 | — | — | — |
| Stomach | 5 | 4 | 4 | 4 | 4 | 5 | 5 | 3 | 3 | — | 5 | — | — | — |
| Multiple myeloma | 4 | 4 | 4 | 5 | 4 | 5 | 4 | 4 | 4 | 4 | 6 | — | — | — |

— Fewer than 3 cases per year.

* 2007 for Canada, Quebec; 2010 for British Columbia, Alberta, Saskatchewan, Manitoba, Ontario, New Brunswick, Nova Scotia, Prince Edward Island, Newfoundland and Labrador; 2006–2010 average for Yukon, Northwest Territories, Nunavut. The numbers of cases from death certificate only for Ontario and Newfoundland and Labrador in 2008–2010 are estimated.

† Canada totals include provincial and territorial estimates.

‡ The number of cases for some cancers used to calculate the overall 2013 estimates for this province was underestimated.

§ Ontario does not currently report *in situ* bladder cancers.

**Note:** Rates for "All cancers" excludes non-melanoma skin cancer (basal and squamous). Rates are age-standardized to the 1991 Canadian population.

**Analysis by:** Chronic Disease Surveillance and Monitoring Division, CCDP, Public Health Agency of Canada
**Data source:** Canadian Cancer Registry database at Statistics Canada

**TABLE A5** Actual data for cancer deaths for the most common cancers by sex and geographic region, Canada, 2009*
(see Statistics Canada CANSIM Table 102-0522 and CANSIM Table 102-0552 for availability of later data releases)

| | Deaths | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Canada† | BC | AB | SK | MB | ON | QC | NB | NS | PE | NL | YT | NT | NU |
| **Males** | | | | | | | | | | | | | | |
| **All cancers** | **37,500** | **4,800** | **3,100** | **1,200** | **1,350** | **13,700** | **10,000** | **1,000** | **1,300** | **180** | **770** | **35** | **25** | **20** |
| Lung | 10,600 | 1,200 | 790 | 300 | 390 | 3,500 | 3,400 | 340 | 350 | 40 | 230 | 10 | 5 | 10 |
| Colorectal | 4,600 | 570 | 380 | 140 | 160 | 1,650 | 1,150 | 110 | 190 | 20 | 130 | 5 | 5 | 5 |
| Prostate | 3,700 | 550 | 370 | 180 | 170 | 1,400 | 780 | 90 | 120 | 25 | 65 | 5 | — | — |
| Pancreas | 2,000 | 310 | 170 | 65 | 60 | 720 | 500 | 55 | 65 | 10 | 25 | — | — | — |
| Non-Hodgkin lymphoma | 1,400 | 210 | 100 | 50 | 40 | 550 | 350 | 40 | 55 | 5 | 20 | — | — | — |
| Leukemia | 1,400 | 160 | 130 | 50 | 60 | 540 | 370 | 25 | 45 | 5 | 10 | — | — | — |
| Bladder | 1,350 | 200 | 100 | 50 | 50 | 500 | 330 | 30 | 35 | 10 | 20 | — | — | — |
| Esophagus | 1,250 | 190 | 120 | 40 | 55 | 520 | 230 | 35 | 50 | 10 | 20 | — | — | — |
| Stomach | 1,200 | 120 | 90 | 30 | 35 | 480 | 310 | 30 | 25 | 5 | 45 | — | — | — |
| Brain | 1,100 | 140 | 95 | 35 | 25 | 440 | 270 | 25 | 45 | 5 | 15 | — | — | — |
| Kidney | 970 | 130 | 95 | 35 | 50 | 330 | 240 | 30 | 25 | 5 | 25 | — | — | — |
| Oral | 720 | 110 | 60 | 15 | 25 | 280 | 170 | 20 | 20 | 5 | 10 | — | — | — |
| Multiple myeloma | 700 | 80 | 70 | 25 | 25 | 260 | 180 | 15 | 25 | 5 | 15 | — | — | — |
| Liver | 650 | 110 | 55 | 10 | 15 | 260 | 160 | 10 | 20 | 5 | 5 | — | — | — |
| Melanoma | 630 | 75 | 55 | 15 | 15 | 290 | 130 | 15 | 30 | — | 15 | — | — | — |
| **Females** | | | | | | | | | | | | | | |
| **All cancers** | **33,700** | **4,200** | **2,700** | **1,000** | **1,300** | **12,400** | **9,100** | **920** | **1,200** | **180** | **610** | **30** | **20** | **20** |
| Lung | 8,500 | 1,050 | 650 | 270 | 310 | 2,900 | 2,500 | 240 | 310 | 50 | 140 | 5 | 5 | 5 |
| Breast | 4,900 | 590 | 400 | 140 | 190 | 1,900 | 1,350 | 130 | 150 | 25 | 75 | 5 | 5 | — |
| Colorectal | 4,000 | 490 | 280 | 110 | 180 | 1,450 | 1,050 | 120 | 160 | 20 | 90 | 5 | 5 | 5 |
| Pancreas | 2,000 | 240 | 170 | 65 | 70 | 750 | 540 | 60 | 70 | 10 | 30 | — | — | — |
| Ovary | 1,600 | 230 | 140 | 45 | 60 | 610 | 390 | 45 | 45 | 5 | 25 | — | — | — |
| Non-Hodgkin lymphoma | 1,200 | 160 | 95 | 40 | 45 | 450 | 300 | 25 | 40 | 5 | 15 | — | — | — |
| Leukemia | 1,100 | 120 | 95 | 30 | 35 | 430 | 270 | 35 | 35 | 5 | 15 | — | — | — |
| Body of uterus | 860 | 85 | 60 | 20 | 40 | 370 | 220 | 10 | 40 | 5 | 10 | — | — | — |
| Brain | 770 | 85 | 65 | 20 | 20 | 290 | 210 | 20 | 30 | 5 | 15 | — | — | — |
| Stomach | 730 | 80 | 55 | 25 | 25 | 270 | 220 | 25 | 20 | 0 | 15 | — | — | — |
| Multiple myeloma | 590 | 65 | 55 | 25 | 15 | 240 | 160 | 15 | 5 | 5 | 10 | — | — | — |
| Bladder | 580 | 85 | 35 | 15 | 25 | 230 | 150 | 10 | 20 | 5 | 10 | — | — | — |
| Kidney | 570 | 65 | 50 | 20 | 30 | 200 | 150 | 15 | 20 | 10 | 15 | — | — | — |
| Esophagus | 420 | 65 | 40 | 15 | 15 | 160 | 80 | 10 | 25 | — | 10 | — | — | — |
| Melanoma | 390 | 55 | 30 | 10 | 10 | 170 | 80 | 10 | 10 | 5 | 10 | — | — | — |
| Cervix | 370 | 30 | 40 | 25 | 20 | 140 | 80 | 10 | 10 | 5 | 10 | — | — | — |
| Oral | 340 | 50 | 35 | 10 | 20 | 130 | 90 | 5 | 10 | — | — | — | — | — |

— Fewer than 3 deaths per year.

* 2005–2009 average for Yukon, Northwest Territories, Nunavut.

† Row totals may not equal the total for Canada due to rounding. Canada totals include provincial and territorial estimates.

**Analysis by:** Chronic Disease Surveillance and Monitoring Division, CCDP, Public Health Agency of Canada
**Data source:** Canadian Vital Statistics Death database at Statistics Canada

**TABLE A6** Actual age-standardized mortality rates (ASMR) for the most common cancers by sex and geographic region, Canada, 2009*
(see Statistics Canada CANSIM Table 102-0522 and CANSIM Table 102-0552 for availability of later data releases)

| | Deaths per 100,000 | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Canada† | BC | AB | SK | MB | ON | QC | NB | NS | PE | NL | YT | NT | NU |
| **Males** | | | | | | | | | | | | | | |
| **All cancers** | **192** | **170** | **182** | **188** | **192** | **185** | **213** | **213** | **214** | **210** | **244** | **268** | **203** | **391** |
| Lung | 54 | 42 | 47 | 49 | 55 | 48 | 71 | 71 | 58 | 45 | 74 | 64 | 50 | 185 |
| Colorectal | 23 | 20 | 23 | 21 | 23 | 22 | 25 | 23 | 32 | 25 | 42 | 38 | 38 | 81 |
| Prostate | 19 | 19 | 22 | 26 | 23 | 19 | 17 | 20 | 21 | 26 | 22 | 29 | — | — |
| Pancreas | 10 | 11 | 10 | 10 | 8 | 10 | 11 | 11 | 11 | 13 | 8 | — | — | — |
| Non-Hodgkin lymphoma | 7 | 8 | 6 | 8 | 6 | 7 | 7 | 9 | 10 | 5 | 6 | — | — | — |
| Leukemia | 7 | 6 | 8 | 8 | 8 | 8 | 8 | 6 | 7 | 4 | 4 | — | — | — |
| Bladder | 7 | 7 | 6 | 8 | 7 | 7 | 7 | 6 | 6 | 10 | 6 | — | — | — |
| Esophagus | 6 | 7 | 6 | 7 | 8 | 7 | 5 | 7 | 8 | 12 | 7 | — | — | — |
| Stomach | 6 | 4 | 5 | 5 | 5 | 6 | 6 | 6 | 5 | 7 | 15 | — | — | — |
| Brain | 6 | 5 | 5 | 5 | 4 | 6 | 6 | 5 | 7 | 6 | 5 | — | — | — |
| Kidney | 5 | 4 | 6 | 6 | 7 | 4 | 5 | 6 | 4 | 5 | 8 | — | — | — |
| Oral | 4 | 4 | 3 | 2 | 3 | 4 | 4 | 4 | 4 | 7 | 3 | — | — | — |
| Multiple myeloma | 4 | 3 | 4 | 4 | 3 | 4 | 4 | 3 | 4 | 4 | 4 | — | — | — |
| Liver | 3 | 4 | 3 | 2 | 2 | 3 | 3 | 2 | 3 | 5 | 1 | — | — | — |
| Melanoma | 3 | 3 | 3 | 2 | 2 | 4 | 3 | 3 | 5 | — | 5 | — | — | — |
| **Females** | | | | | | | | | | | | | | |
| **All cancers** | **137** | **123** | **130** | **131** | **150** | **132** | **148** | **151** | **151** | **164** | **161** | **214** | **174** | **330** |
| Lung | 36 | 33 | 33 | 37 | 37 | 32 | 43 | 42 | 41 | 48 | 38 | 54 | 49 | 156 |
| Breast | 20 | 18 | 19 | 18 | 22 | 20 | 22 | 22 | 20 | 24 | 19 | 19 | 20 | — |
| Colorectal | 15 | 14 | 13 | 12 | 19 | 14 | 16 | 17 | 19 | 18 | 23 | 28 | 30 | 52 |
| Pancreas | 8 | 7 | 8 | 8 | 7 | 8 | 9 | 9 | 9 | 6 | 8 | — | — | — |
| Ovary | 7 | 7 | 7 | 6 | 7 | 7 | 6 | 8 | 5 | 5 | 7 | — | — | — |
| Non-Hodgkin lymphoma | 5 | 5 | 4 | 5 | 5 | 5 | 5 | 4 | 5 | 5 | 3 | — | — | — |
| Leukemia | 4 | 3 | 5 | 4 | 4 | 4 | 4 | 6 | 4 | 4 | 5 | — | — | — |
| Body of uterus | 4 | 3 | 3 | 3 | 4 | 4 | 4 | 2 | 5 | 4 | 3 | — | — | — |
| Brain | 3 | 3 | 3 | 3 | 3 | 3 | 4 | 4 | 4 | 4 | 4 | — | — | — |
| Stomach | 3 | 2 | 3 | 3 | 3 | 3 | 3 | 4 | 2 | 1 | 3 | — | — | — |
| Multiple myeloma | 2 | 2 | 3 | 3 | 1 | 2 | 3 | 2 | 1 | 6 | 3 | — | — | — |
| Kidney | 2 | 2 | 2 | 3 | 3 | 2 | 2 | 2 | 2 | 8 | 4 | — | — | — |
| Bladder | 2 | 2 | 1 | 1 | 2 | 2 | 2 | 2 | 2 | 4 | 3 | — | — | — |
| Cervix | 2 | 1 | 2 | 4 | 3 | 2 | 1 | 2 | 1 | 5 | 2 | — | — | — |
| Esophagus | 2 | 2 | 2 | 2 | 2 | 2 | 1 | 2 | 3 | — | 2 | — | — | — |
| Melanoma | 2 | 2 | 1 | 1 | 1 | 2 | 1 | 2 | 2 | 3 | 2 | — | — | — |
| Oral | 1 | 1 | 2 | 1 | 2 | 1 | 1 | 1 | 1 | — | — | — | — | — |

— Fewer than 3 deaths per year.

* 2005–2009 average for Yukon, Northwest Territories, Nunavut.

† Canada totals include provincial and territorial estimates.

**Note:** Rates are age-standardized to the 1991 Canadian population.

**Analysis by:** Chronic Disease Surveillance and Monitoring Division, CCDP, Public Health Agency of Canada
**Data source:** Canadian Vital Statistics Death database at Statistics Canada

# APPENDIX II: Data sources and methods

## Data sources

### Incidence data: The Canadian Cancer Registry (CCR)

Actual cancer incidence data used in this publication cover the period of 1984 to 2010 (except for Quebec, for which data from the CCR were available for 1983 to 2007 in time for this publication). Data for 1992 to 2010 were obtained from the CCR[1] (September 2012 CCR Tabulation Master File), while data for earlier years were retrieved from its predecessor, the National Cancer Incidence Reporting System (NCIRS). The NCIRS is a fixed, tumour-oriented database containing cases diagnosed as far back as 1969.

- Incidence data originate with the provincial and territorial cancer registries, which provide data annually to Statistics Canada for inclusion in the CCR.
- The CCR is a person-oriented database that includes clinical and demographic information about residents of Canada newly diagnosed with cancer.
- The Health Statistics Division at Statistics Canada maintains the CCR. It links data internally to identify duplicate person and tumour records. The Health Statistics Division also links cancer data with mortality data (described below) to ensure the completeness and correctness of vital status information and capture missed cancer cases. Both linking procedures optimize the accuracy of incidence, prevalence and survival statistics.
- Cancer diagnoses are classified according to the *International Classification of Diseases for Oncology, Third Edition* (ICD-O-3).[2]
- *Chapter 7: Special topic: Liver cancer* uses incidence data from 1970 onwards.

### Mortality data: The Canadian Vital Statistics — Death database (CVS: D)

- The actual cancer mortality data cover the period of 1984 to 2009 and were obtained from the CVS: D.[3]
- Death records originate with the provincial and territorial registrars of vital statistics and are provided regularly to Statistics Canada for inclusion in the CVS: D.
- The CVS: D includes demographic and cause of death information for all residents who died in Canada between 1950 and 2009.
- Data are also included for Canadian residents who died in some states of the United States, as Canada currently receives abstracted death data from approximately 10 states.
- The Health Statistics Division at Statistics Canada maintains the CVS: D.
- Cause of death is classified according to the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision* (ICD-10).[4]
- Cancer deaths are those for which some form of cancer, as certified by a physician, is the underlying cause of death.
- *Chapter 7: Special topic: Liver cancer* uses mortality data from 1970 onwards.

### Population data: The Census of Canada

- Population estimates for Canada and the provinces and territories are based on censuses conducted every five years from 1981 through to 2006.
- Intercensal estimates prepared by Statistics Canada are used for the years between these censuses, and postcensal estimates are used for 2006 to 2011.[5]
- Projected population estimates are used for 2012 and 2013, as prepared by Statistics Canada under assumptions of medium growth (scenario M1).[6] The scenario M1 incorporates medium-growth and historical trends (1981 to 2008) of interprovincial migration.
- All population estimates include non-permanent residents and are adjusted for net census under-coverage and Canadians returning from abroad.

### Life tables

- Life tables are required to estimate relative survival. Sex-specific provincial life tables are produced by Statistics Canada.
- Data from the 1990 to 1992 life tables[7] were used for follow-up in 1992 and 1993. Data from 1995 to 1997 life tables[8] were used for follow-up from 1994 to 1998. Data from the 2000 to 2002 life tables[9] were used for follow-up from 1999 to 2003. Data from the 2005 to 2007 life tables were used for follow-up from 2004 to 2008.[10]

- Complete life tables were not available for Prince Edward Island or the territories, so expected survival proportions for these areas were derived from abridged life tables for Canada, Prince Edward Island and the territories using a method suggested by Dickman et al.[11] Where this was not possible (i.e., for the territories from 1990 to 1992), complete Canadian life table values were used.
- The method of Dickman et al. was also used to extend, by single year of age, the 1990 to 1992 set of provincial life tables for people aged 85–99 years.

### Cancer definitions

- Cancers are generally defined according to the groupings of ICD-O-3[2] for incidence and ICD-10[4] for mortality (Table A7).
- Some definitions have changed slightly over time; changes occurring since the 2004 edition of this publication are outlined in Tables A8-1 and A8-2.
- For children and youth aged 0–14 years, cancers were classified and reported according to the *International Classification of Childhood Cancer, Third Edition* (ICCC-3).[12] This system is most appropriate for reporting childhood cancers because it acknowledges the major differences between cancers that develop during childhood and those that occur later in life.
- The category "intracranial and intraspinal" excludes non-malignant tumours.
- Bladder cancer includes bladder *in situ* carcinomas, which are considered invasive for the purpose of incidence reporting and are included for provinces and territories except Ontario.

## Methods

### Incidence and mortality rates

Records from each province or territory were extracted from the relevant incidence or mortality files and then classified by year of diagnosis or death and by sex, five-year age group (0–4, 5–9,…, 80–84 and 85+ years) and cancer type.

- Rates for each category were calculated by dividing the number of cases or deaths in each category (i.e., province or territory, year, sex, age group, cancer type) by the corresponding provincial or territorial population figure. These formed the basis for calculations of age-standardized rates and for estimates beyond the most recent year of actual data.
- For the section *Incidence and mortality by age and sex*, age-specific rates were computed for broader age groups (0–19, 20–29, …, 70–79 and 80+ years) in the same way.
- Age-standardized incidence rates (ASIR) and mortality rates (ASMR) were calculated using the direct method, which involves weighting the age-specific rates for each five-year age group according to the age distribution of the 1991 Canadian population:

1991 Canadian standard population

| Age group | Population (per 100,000) |
|---|---|
| 0–4 | 6,946.4 |
| 5–9 | 6,945.4 |
| 10–14 | 6,803.4 |
| 15–19 | 6,849.5 |
| 20–24 | 7,501.6 |
| 25–29 | 8,994.4 |
| 30–34 | 9,240.0 |
| 35–39 | 8,338.8 |
| 40–44 | 7,606.3 |
| 45–49 | 5,953.6 |
| 50–54 | 4,764.9 |
| 55–59 | 4,404.1 |
| 60–64 | 4,232.6 |
| 65–69 | 3,857.0 |
| 70–74 | 2,965.9 |
| 75–79 | 2,212.7 |
| 80–84 | 1,359.5 |
| 85+ | 1,023.7 |
| **Total** | **100,000** |

Figure B (*Introduction*) shows the number of deaths avoided since the mortality rate for all cancers combined peaked in 1988.

- The year 1988 was chosen as the baseline year when the overall cancer mortality rate was at its highest for Canadian men and women.
- The age-specific cancer mortality rates from 1988 for males and females in each five-year age group were applied to the age-specific populations for each of the subsequent years up to 2007 to obtain the expected number of deaths for each of those years if the 1988 death rates prevailed.
- To obtain the excess deaths that would have occurred, the expected deaths for each year were summed and then the observed number of deaths for each year was subtracted from this total.

Figure C (*Introduction*) shows the relative contributions to the changes in the total number of new cases and deaths that can be attributed to changes in cancer risk and cancer control practices, population size and aging of the population.

- The lowest solid line represents the total number of new cancer cases (or deaths) that would have occurred each year if the population size and age structure had remained the same as they were in 1984. This line reflects the impact of changes in cancer risk and cancer control practices.
- The middle line represents the number of new cases (or deaths) that would have occurred if the age structure of the population had remained the same as it was in 1984. This line reflects the impact of changes in cancer risk and population growth.
- The top line represents the number of new cases (or deaths) that actually occurred and thus reflects the combined impact of changes in risk, population growth and aging of the population.

The series shown in Figure C were calculated as follows:

- Uppermost series: the annual number of Canadian cancer cases or deaths, for males or females
- Next-to-uppermost series: annual total population multiplied by the annual age-standardized rate, using the 1984 population distribution for males or females as the standard weights
- Next-to-baseline series: the 1984 total population multiplied by the annual age-standardized rate, using the 1984 population distribution for males or females as the standard weights
- Baseline (dotted line): the observed number of Canadian cancer cases or deaths during 1984, for males or females.

## Estimation of incidence (new cases) and mortality (deaths) for 2013

Two methods were used to estimate incidence and mortality data: the Nordpred Power5 regression model and five-year averaging.

### Nordpred Power5 modelling

The Nordpred Power5 regression model was the primary method for estimating the number of new cases and deaths in 2013 for each cancer type by sex (except new cases of prostate cancer and non-melanoma skin cancer; see *Prostate cancer incidence* and *Non-melanoma skin cancer incidence* below) reported in Tables 1.2 and 3.2. Nordpred is based on an age-period-cohort Poisson regression model but has enhancements that overcome difficulties in the standard Poisson model and improve projection accuracy.[13] Nordpred was developed into a software package[14] and is now one of the most frequently used methods for cancer projections worldwide.[15–19]

The Nordpred Power5 regression model was used when the average annual number of cases for a type of cancer for the most recent five years was greater than 50. The assumption underlying the Nordpred Power5 regression model is that the annual number of new cases and deaths are independent Poisson random variables with mean values equal to the product of the population size for a particular year and the (true) annual rate.

- A separate Nordpred Power5 regression model was fit for each province, sex and type of cancer for the period of 1986 to 2010 (1983 to 2007 for Quebec) for incidence and 1985 to 2009 for mortality.
- The Nordpred Power5 regression model is $R_{ap} = (A_a + D \cdot p + P_p + C_c)^5$ where *a, p* and *c* represent age, period and cohort, respectively, in five-year groups. Input data were aggregated into five-year calendar periods and 18 five-year age groups (described above); cohorts were created synthetically by subtracting age from period. $R_{ap}$ is the incidence/mortality rate in age group *a* in calendar period *p*, $A_a$ is the age component for age group *a*, *D* is the common linear drift parameter of period and cohort.[20] $P_p$ is the nonlinear period component of period *p*, and $C_c$ is the nonlinear cohort component of cohort *c*.
- Nordpred uses a goodness of fit test to choose the number of five-year periods to be included in the dataset used for calculating future values (projection base).
- The software determines whether the average trend across all observed values, or the slope for the last 10 years of observed values, is used for projection, based on a significance test for departure from linear trend. This approach serves as an approximate way of looking for significant changes in the observed trend. The software also allows the user to make this selection.
- For each age group, a minimum of five cases in each five-year period was required; for age groups below this limit, the average number of cases in the last two periods is used to calculate future rates.
- To allow for a damping of the impact of current trends in the future time periods, a "cut-trend" option is used, which is a vector of proportions indicating how much to cut the trend estimate for each five-year projection period. A gradual reduction in the drift parameter of 25% and 50% in the second and third five-year period, respectively, was used as the default in this publication.

- Age was included in all models as a factor. Age-specific incidence rate trends were then extrapolated to 2013. The predicted numbers of cancer cases in 2013 were calculated by multiplying these extrapolated incidence rates by the sex-, age- and province-specific population projections for the same year.
- The Nordpred "recent" and "cut-trend" options were modified from the default values for selected types of cancer, including thyroid cancer incidence and prostate cancer mortality, since recent trends are not expected to continue with as large an annual percent change. The values were chosen so that estimates were consistent with the most recent data available to the provincial cancer registries.

### Five-year averaging

New cases and deaths in 2013 for each type of cancer were also estimated based on the average of the five most recent years of data. This method may be more realistic for cancers for which there are recent changes in trend (the Nordpred Power5 regression model results in poor estimates for these cancers because it is based on a medium or longer term trend) or when frequencies are low and result in unstable estimates using the Nordpred model. The average of rates for the most recent five years was calculated for each sex, five-year age group, cancer type and province. The predicted numbers were then obtained by multiplying these rates by the corresponding projected population sizes.

### Selection of "best" estimates

Estimates from the two methods were compared for each sex, cancer type and geographic region for all ages combined. The "best" estimate for each category was selected in consultation with individual provincial or territorial cancer registries, according to the following guidelines:

- The Nordpred model was preferred except when frequencies were low.
- Five-year average estimates were used when the average annual number of cases during the most recent five years was less than or equal to 50.
- Five-year average estimates were used for the territories and are reported only for "all cancers" because of small sample sizes.
- The absolute value of the difference between the age-standardized rates estimated by the two methods was calculated and expressed relative to the five-year average estimate. For example, if the Nordpred Power5 regression model estimated a rate of 4.0 and the five-year average estimated a rate of 4.5, the relative difference would be $|4.0 - 4.5| \div 4.5$, or 11.1%.
- Provinces closely examined estimates for cancers where the absolute value of the relative difference exceeded 15%. Such situations may be indicative of important deviations from the long-term trend.
- Provinces provided feedback based on the availability of in-house projections, knowledge of local trends or access to more current data, which permitted an assessment of the estimates produced by the two different estimation methods.
- Estimates for Canada as a whole were computed as sums of the estimates for the individual provinces and territories.

Tables A9 and A10 indicate the cancer types that were reported according to the five-year average method for 2013. In these situations, the age-standardized rates for 2013 reported in this publication were calculated using the most recent five years of actual data.

### All cancers combined

Provincial estimates of incidence counts for "all cancers" for males were computed as the sum of the "best" estimates for prostate cancer and all cancers excluding prostate, as estimated by the Nordpred modelling.

### Prostate cancer incidence

The results of the Nordpred Power5 regression model are not satisfactory for prostate cancer. An annual age-specific trend Power5 projection model was fitted to a minimum of seven and a maximum of nine years of data, as selected by a goodness of fit test. The model is $R_{ap} = (A_a + D_a \cdot p)^5$, where $a$ is age, $p$ is period, $A_a$ is the age effect of age group $a$, $D_a$ is the slope parameter at the $a$th age group, which takes the differentiation in trend from different 10-year age groups into consideration.

New cases of prostate cancer in 2013 were also estimated based on the most recent year of data available. This method may be more realistic when there are recent changes in trend (the age-specific trend model results in poor estimates for prostate cancers because it is based on a medium-term trend). The predicted numbers were then obtained by multiplying these rates by the corresponding projected population sizes.

## Non-melanoma skin cancer incidence

Only a few provinces routinely collect data on the incidence of basal cell and squamous cell carcinoma of the skin (generally referred to as non-melanoma skin cancer, or NMSC). The numbers of NMSC in all of Canada, by sex, were estimated using these data.

- Pathology laboratories in British Columbia send all diagnostic reports of NMSC to the provincial registry. The age- and sex-specific incidence rates in British Columbia for 1992 to 1994 and 2003 were projected to 2013 by the British Columbia Cancer Registry and applied to the projected Canadian population estimates to generate an estimate of the number of cases for Canada as a whole.
- Counts of NMSC for 1992 to 2010 by year, sex and age group were provided by the Manitoba Cancer Registry and by the New Brunswick Cancer Registry. Linear regressions using a logarithmic transformation of the annual rates for each province and age group (0–39, 40–59, 60–79 and 80+ years) were conducted and projected to 2013. The predicted numbers of NMSC cases for all of Canada were calculated by multiplying the projected incidence rates for each of Manitoba and New Brunswick by the sex- and age-specific Canadian population projections for 2013.
- Reported new cases of NMSC for all of Canada are the average of 2013 estimates from British Columbia, Manitoba and New Brunswick registries.

## Rounding for reporting

- Estimates of incidence and mortality presented in this publication have been rounded as follows:
  - Numbers between 0 and 99 were rounded to the nearest 5.
  - Numbers between 100 and 999 were rounded to the nearest 10.
  - Numbers between 1,000 and 1,999 were rounded to the nearest 50.
  - Numbers greater or equal to 2,000 were rounded to the nearest 100.
- Percentages, age-standardized rates and age-specific rates were rounded to the nearest 10th, except in Tables 2.5, 4.5, A4 and A6, where space restrictions forced rounding to the nearest whole number.
- Age-specific and sex-specific numbers or rates were combined before rounding, so it is possible that the totals in the tables do not add up. However, any such discrepancies are within the precision of the rounding units described above.

## Precision of 2013 estimates

Estimates of precision (standard errors, coefficients of variation and confidence limits) for 2013 counts and rates are available on request from the Chronic Disease Surveillance and Monitoring Division (Centre for Chronic Disease Prevention, Public Health Agency of Canada). The precision of an estimate depends primarily on the number of observed cases and the population size for each combination of cancer type, age, sex and province or territory.

## Annual percent change (APC) in cancer incidence and mortality rates

The estimated APC was calculated for each cancer type by fitting a piecewise linear regression model, assuming a constant rate of change in the logarithm of the annual ASIR or ASMR in each segment. The models incorporated estimated standard errors of the ASIR or ASMR. The tests of significance used a Monte Carlo Permutation method. The estimated slope from this model was then transformed back to represent an annual percentage increase or decrease in the rate.

- Joinpoint analysis was applied to annual age-standardized rates over the period of 1986 to 2007 (for incidence) and 1986 to 2009 (for mortality) to determine years in which the APC changed significantly; such years are referred to as *changepoints*.
- A minimum of five years of data before and after a changepoint was required for a new trend to be identified. Thus, the most recent possible changepoint is 2003 for incidence and 2005 for mortality.
- If no changepoint was detected within the periods of 1998 to 2007 (for incidence) or 2000 to 2009 (for mortality), then the APC was estimated by fitting a model within these time periods, in the same way as described above.
- If a changepoint was detected within these decades, then the APC was estimated from the trend in the last segment. Both the changepoint year and the APC for the years beyond the changepoint are indicated in Tables 1.5 and 3.5.
- Changepoints in incidence rates for 1970 to 2007 and mortality rates for 1970 to 2009 for liver cancer are reported in *Chapter 7: Special topic: Liver cancer*.

## Probability of developing or dying from cancer

Probabilities of developing or dying from cancer were calculated according to the age- and sex-specific cancer incidence and mortality rates for Canada in 2007 and life tables based on all-cause mortality rates from 2006 to 2008. The methodology used was that of Zdeb[21] and Seidman et al.[22]

- The method used for the probability of developing cancer assumes that current age-specific incidence rates will prevail throughout the future lifetime of a person as he or she advances in age. Since this assumption may not be true, the probabilities should be regarded only as approximations.
- The probability of dying from cancer represents the proportion of people who die of cancer in a cohort subjected to the mortality conditions prevailing in the population at large in 2007. It was estimated by determining the proportion of deaths attributed to specific types of cancer for each sex and age group, multiplying this proportion by the corresponding number of deaths in the life table and summing the life table deaths over all sex and age groups to obtain the probability of dying from each cause.

## Relative survival

Five-year relative survival ratios (RSRs) were estimated by comparing the actual survival experience of persons diagnosed with cancer to that expected in the general population of Canadians of the same age, sex, province of residence and time period. It is computed as a ratio and expressed as a percentage.

- Deaths of people diagnosed with cancer are identified through record linkage of the CCR to the CVS: D, and from information reported by provincial or territorial cancer registries. For deaths reported by a registry but not confirmed by record linkage, it was assumed that the individual died on the date submitted by the reporting province or territory. At the time of the analysis, registration of new cases and follow-up for vital status were complete through December 31, 2008.
- Analyses were based on all primary cancers. The effect of including multiple cancers in survival analyses has been studied both internationally[23,24] and in Canada.[25]
- Analyses were based on those individuals aged 15–99 years at diagnosis.
- Persons whose diagnosis was established through death certificate only or autopsy only were excluded.
- Analyses were based on a publicly available algorithm,[26] with some minor adaptations. Expected survival proportions were derived, using the Ederer II approach,[27] from sex-specific provincial life tables produced by Statistics Canada.
- Survival analyses were conducted using both period (2006 to 2008) and cohort (1992 to 1994) analysis methods.[28] The period approach to survival analysis provides up-to-date predictions of cancer survival.[29] With this method, follow-up data do not relate to a fixed cohort of people with cancer. Rather, estimates of period survival are based on the assumption that persons diagnosed in the period of interest will experience the most recently observed conditional probabilities of survival. When survival is generally improving, a period estimate tends to be a conservative prediction of the survival that is eventually observed.
- Conditional five-year relative survival expresses the probability of surviving five years into the future at various points since the time of diagnosis, relative to the expected survival of a comparable group in the general population.[30,31] It is calculated as per five-year RSRs, except conditional RSRs are estimated using people who have survived certain amounts of time after the date of cancer diagnosis.
- As an indication of the level of statistical uncertainty in the survival estimates, confidence intervals formed from standard errors estimated using Greenwood's method[32] are provided. To avoid implausible lower limits less than zero or upper limits greater than one for observed survival estimates, asymmetric confidence intervals based on the log (–log) transformation were constructed. RSR confidence limits were derived by dividing the observed survival limits by the corresponding expected survival proportion.
- Age-standardized estimates were calculated using the direct method by weighting age-specific estimates for a given cancer to the age distribution of persons diagnosed with that cancer from 1992 to 2001. Confidence intervals for age-standardized RSRs were formed by multiplying the corresponding age-standardized observed upper and lower limits by the ratio of the age-standardized relative survival point estimate to the age-standardized observed survival point estimate.

### Prevalence

The primary type of prevalence reported in this publication is tumour based. Two-, five- and 10-year limited duration prevalences are estimated by the numbers of cancers diagnosed in the previous two, five and 10 years among people with cancer who are alive.

Estimating prevalence requires current, accurate information about both the incidence and vital status of cases. Because of issues in correctly ascertaining the vital status of persons diagnosed while residing in Quebec, the following approach was used:

- Cancer site-, sex- and age-specific limited duration prevalences for all of Canada, excluding Quebec, were determined directly using the counting method.[33,34] Specifically, all primary invasive cancers (including *in situ* bladder cancers) diagnosed among persons residing outside of Quebec in the relevant time period and alive on January 1, 2009, were counted, regardless of whether they were first or subsequent primaries.
- Sex- and age-specific population estimates for January 1, 2009, were derived by averaging the 2008 and 2009 mid-year population estimates for all of Canada, excluding Quebec.
- Cancer site-, sex- and age-specific limited duration prevalence proportions for all of Canada, excluding Quebec, were then estimated by dividing counts by the appropriate population estimates.
- Cancer site-, sex- and age-specific counts for all of Canada, including Quebec, were then obtained by applying the prevalence proportions to Canadian sex- and age-specific population estimates, which included Quebec, and then summing across the strata.
- Person-based limited duration prevalences are estimated as the number of individuals represented in the tumour-based limited duration prevalences.
- Age-specific prevalence estimates were obtained using the age attained as of January 1, 2009.

The above approach for estimating cancer prevalence in Canada is different from that employed in previous versions of this publication. The current approach's primary assumption is that sex- and age-specific limited duration cancer prevalence proportions, calculated using cancer cases and population estimates from all of Canada excluding Quebec, are an accurate estimate of cancer prevalence proportions within Quebec.

## Data and methods issues

### Incidence

Although the Canadian Council of Cancer Registries and its Standing Committee on Data Quality make every effort to achieve uniformity in defining and classifying new cancer cases, reporting procedures and completeness still vary across the country. The standardization of case-finding procedures, including linkage to provincial or territorial mortality files, has improved the registration of cancer cases and comparability of data across the country. Some specific issues remain:

- Benign tumours and carcinomas *in situ* are not routinely captured or reported except for *in situ* carcinomas of the bladder; all cancer registries except Ontario report *in situ* bladder cancers to the CCR.
- There may be under-reporting of cancer cases in Newfoundland and Labrador due to incomplete linkage of cancer data with death data. This under-reporting could result in death counts or rates exceeding those for incidence in a specific year; this especially affects highly fatal cancers. The number of "death certificate only" (DCO) cases for 2008 to 2010 in Newfoundland and Labrador was estimated from 2007 data.
- In Quebec, cases diagnosed through DCO are incompletely captured prior to 2000. In addition, because of the registry's dependence on hospital data for the period included in the present report, the numbers of cases of some cancers are underestimated, particularly for those where pathology reports represent the main source of diagnostic information. Prostate cancer, melanoma and bladder cancer are affected in particular.[35] The 2013 estimates for these sites may be an underestimate because an increase in cases in the registry is expected with the inclusion of pathology reports starting with 2011 data.
- The number of DCO cases for 2008, 2009 and 2010 in Ontario was estimated from the average of 2003 to 2007 data.
- The number of DCO cases is less than 2% of total cases.
- Non-melanoma skin cancers are excluded since most provincial and territorial cancer registries do not collect information on these cases. These cancers are difficult to register completely because they may be diagnosed and treated in a variety of settings and are very numerous. Estimates based on the three registries that include these cancers (see *Non-melanoma skin cancer incidence* above) are therefore likely to be underestimates.

## Mortality

Although procedures for registering and allocating cause of death have been standardized both nationally and internationally, some lack of specificity and uniformity is inevitable. The description of cancer type provided on the death certificate is usually less accurate than that obtained by the cancer registries from hospital and pathology records.

Although there have been numerous small changes in definitions over the years (see Tables A8-1 and A8-2), there is one major earlier change of note:

- In the versions of this publication published before 2003, mortality due to colorectal cancer was based on the *International Classification of Diseases, Ninth Revision* (ICD-9),[36] codes 153–154, to be consistent with other publications. However, this underestimates colorectal cancer mortality by about 10% because most deaths registered as ICD-9 code 159.0 (intestine not otherwise specified) are cases of colorectal cancer.
- Commencing with the 2003 edition, these deaths were included in the definition of colorectal cancer. As a consequence, mortality figures for colorectal cancer appearing in this publication cannot be directly compared with those appearing in publications prior to 2003.

## Survival

Cases diagnosed in the province of Quebec were excluded from survival analyses, in part because the method of ascertaining the date of diagnosis of cancer cases in this province clearly differed from that of the other provincial cancer registries,[37] and because of issues in correctly ascertaining the vital status of cases.

## Prevalence

Because of issues in correctly ascertaining the vital status of persons diagnosed while residing in Quebec, prevalence data for this province were determined indirectly (see the *Methods* section above). Prevalence estimates were derived using the corresponding observed prevalence proportion calculated for the rest of Canada, stratified on age group, sex and cancer type.

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**TABLE A7** Cancer definitions

| Cancer | ICD-O-3 Site/Type (incidence) | ICD-10 (mortality) |
|---|---|---|
| Oral | C00–C14 | C00–C14 |
| Esophagus | C15 | C15 |
| Stomach | C16 | C16 |
| Colorectal | C18–C20, C26.0 | C18–C20, C26.0 |
| Liver | C22.0 | C22.0, C22.2–C22.7 |
| Pancreas | C25 | C25 |
| Larynx | C32 | C32 |
| Lung | C34 | C34 |
| Melanoma | C44 (Type 8720–8790) | C43 |
| Breast | C50 | C50 |
| Cervix | C53 | C53 |
| Body of uterus | C54–C55 | C54–C55 |
| Ovary | C56.9 | C56 |
| Prostate | C61.9 | C61 |
| Testis | C62 | C62 |
| Bladder (including *in situ*) | C67 | C67 |
| Kidney | C64.9, C65.9 | C64–C65 |
| Brain | C70–C72 | C70–C72 |
| Thyroid | C73.9 | C73 |
| Hodgkin lymphoma* | Type 9650–9667 | C81 |
| Non-Hodgkin lymphoma* | Type 9590–9597, 9670–9719, 9724–9729, 9735, 9737, 9738<br>Type 9811–9818, 9823, 9827, 9837 all sites except C42.0,.1,.4 | C82–C85, C96.3 |
| Multiple myeloma* | Type 9731, 9732, 9734 | C90.0, C90.2 |
| Leukemia* | Type 9733, 9742, 9800–9801, 9805–9809, 9820, 9826, 9831–9836, 9840, 9860–9861, 9863, 9865–9867, 9869–9876, 9891, 9895–9898, 9910, 9911, 9920, 9930–9931, 9940, 9945–9946, 9948, 9963–9964<br>Type 9811–9818, 9823, 9827, 9837 sites C42.0,.1,.4 | C91–C95, C90.1 |
| All other cancers | All sites C00–C80, C97 not listed above | All sites C00–C80, C97 not listed above |
| All other and unspecified cancers (grouping used only in Tables A1 and A2) | Type 9140, 9740, 9741, 9750–9759, 9760–9769, 9950–9962, 9966, 9970–9989, 9991, 9992<br>C76.0–C76.8 (type 8000–9592)<br>C80.9 (type 8000–9592)<br>C42.0–C42.4 (type 8000–9592)<br>C77.0–C77.9 (type 8000–9592)<br>C44.0–C44.9 excluding type 8050–8084, 8090–8110, 8720–8790, 9590–9992 | C26.1, C44, C46, C76–C80, C88, C96.0–.2, C96.7–.9, C97 |
| All cancers | All invasive sites | All invasive sites |

* Histology types 9590–9992 (leukemia, lymphoma and multiple myeloma), 9050–9055 (mesothelioma) and 9140 (Kaposi sarcoma) are excluded from other specific organ sites.

**Note:** ICD-O-3 refers to the *International Classification of Diseases for Oncology, Third Edition*.[2] ICD-10 refers to the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision*.[4]

**TABLE A8-1** Recent cancer definition changes in incidence

| | New definition | Year changed | Old definitions |
|---|---|---|---|
| Bladder | ICD-O-3 C67 (including *in situ* cancers, except for Ontario since this province does not report *in situ* bladder cancer) | 2006 | ICD-O-3, C67 (not including *in situ* cancers) |
| Colorectal | ICD-O-3 C18–C20, C26.0 | 2011 | ICD-O-3 C18–C21, C26.0 |
| Kidney | ICD-O-3 C64–C65 | 2008 | ICD-O-3 C64–C66, C68 |
| Lung | ICD-O-3 C34 | 2008 | ICD-O-3 C33-C34 (before 2006)<br>ICD-O-3 C34 (in 2006)<br>ICD-O-3 C33–C34 (in 2007) |
| Ovary | ICD-O-3 C56 | 2006 | ICD-O-3 C56, C57.0–C57.4 |

**Note:** According to ICD-O-3, incidence for bladder, colorectal, kidney, lung and ovary cancers excludes histology types 9590–9992 (leukemia, lymphoma and multiple myeloma), 9050–9055 (mesothelioma) and 9140 (Kaposi sarcoma). ICD-O-3 refers to the *International Classification of Diseases for Oncology, Third Edition*.[2]

**TABLE A8-2** Recent cancer definition changes in mortality

| | New definition | Year changed | Old definitions |
|---|---|---|---|
| Colorectal | ICD-10 C18–C20, C26.0 | 2012 | ICD-10 C18–C21, C26.0 |
| Kidney | ICD-10 C64–C65 | 2008 | ICD-10 C64–C66, C68 |
| Leukemia | ICD-10 C91–C95, C90.1 | 2008 | ICD-10 C91–C95 |
| Liver | ICD-10 C22.0, C22.2–C22.7 | 2007 | ICD-10 C22 (before 2006)<br>ICD-10 C22.0, C22.2–C22.9 (in 2006) |
| Lung | ICD-10 C34 | 2008 | ICD-10 C33–C34 (before 2006)<br>ICD-10 C34 (in 2006)<br>ICD-10 C33–C34 (in 2007) |
| Multiple myeloma | ICD-10 C90.0, C90.2 | 2008 | ICD-10 C88, C90 (before 2007)<br>ICD-10 C90 (in 2007) |
| Ovary | ICD-10 C56 | 2006 | ICD-10 C56, C57.0–C57.4 |
| All other and unspecified cancers | ICD-10 C44, C46, C76–C80, C88,C96.0–C96.2, C96.7–C96.9, C97 | 2007 | ICD-10 C44, C46, C76–C80,C96.0–C96.2, C96.7–C96.9, C97 |

**Note:** ICD-10 refers to the *International Statistical Classification of Diseases and Related Health Problems, Tenth Revision*.[4]

**TABLE A9** Use of five-year average method* for incidence projection by cancer type, sex and province, 2013

| | BC | | AB | | SK | | MB | | ON | | QC | | NB | | NS | | PE | | NL | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | M | F | M | F | M | F | M | F | M | F | M | F | M | F | M | F | M | F | M | F |
| All cancers | | | | | | | | | | | | | | | | ● | | | | |
| Lung | | | | | | | | | | | | | | | | | | | | |
| Breast | | | | | | | | | | | | | | | | | | | | |
| Colorectal | | | | | | | | | | | | | | | | | | ● | | |
| Prostate† | | | | | ■ | | | | | | ■ | | ■ | | | | | | ■ | |
| Bladder | | | | | | | | | | | | | | | | | ■ | ● | | ● |
| Non-Hodgkin lymphoma | | | | | | | ■ | | | | | | | | ■ | | ■ | ● | | |
| Melanoma | | | | | | | | | | | | | | | | | ■ | ● | ■ | ● |
| Kidney | | | | | | | | ● | | | | | | | | | ■ | ● | | ● |
| Leukemia | | | | | | | | | | | | | | ● | | | ■ | ● | ■ | ● |
| Thyroid | | | | | ■ | ● | ■ | | | | | | ■ | | ■ | | ■ | ● | ■ | ● |
| Body of uterus | | | | | | | | | | | | | | | | | | ● | | |
| Pancreas | | | | | | | | | | | | | | | | | ■ | ● | ■ | ● |
| Oral | | | | | | ● | | ● | | | | | | ● | | ● | ■ | ● | ■ | ● |
| Stomach | | | | | | ● | | ● | | | | | | ● | | ● | ■ | ● | | ● |
| Brain | | | | | ■ | ● | ■ | ● | | | | | ■ | ● | ■ | ● | ■ | ● | ■ | ● |
| Ovary | | | | | | | | | | | | | | | | | | ● | | ● |
| Multiple myeloma | | | | | ■ | ● | ■ | ● | | | | | ■ | ● | ■ | ● | ■ | ● | ■ | ● |
| Liver | | | | ● | ■ | ● | ■ | ● | | | | | ■ | ● | ■ | ● | ■ | ● | ■ | ● |
| Esophagus | | | | ● | ■ | ● | ■ | ● | | | | | ■ | ● | ■ | ● | ■ | ● | ■ | ● |
| Cervix | | | | | | ● | | ● | | | | | | ● | | ● | | ● | | ● |
| Larynx | | ● | | ● | ■ | ● | ■ | ● | | | | | ■ | ● | ■ | ● | ■ | ● | ■ | ● |
| Hodgkin lymphoma | | ● | ■ | ● | ■ | ● | ■ | ● | | | | | ■ | ● | ■ | ● | ■ | ● | ■ | ● |
| Testis | | | | | ■ | | ■ | | | | | | ■ | | ■ | | ■ | | ■ | |

M = males; F = females. BC = British Columbia; AB = Alberta; SK = Saskatchewan; MB = Manitoba; ON = Ontario; QC = Quebec; NB = New Brunswick; NS = Nova Scotia; PE = Prince Edward Island; NL = Newfoundland and Labrador.

* Nordpred Power5 regression model is the default for all provinces except when the average annual cases for the most recent five years is less than or equal to 50, when the five-year average estimate is the default.

† An annual age-specific trend Power5 projection model is the default for prostate cancer. In place of the five-year average as an alternative, the last available year of data was used for prostate cancer to better capture recent changes observed for this cancer.

**Note:** For territories (not shown), five-year average method was used for "All cancers" because of small numbers.

**TABLE A10** Use of five-year average method* for mortality projection by cancer type, sex and province, 2013

| | BC | | AB | | SK | | MB | | ON | | QC | | NB | | NS | | PE | | NL | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | M | F | M | F | M | F | M | F | M | F | M | F | M | F | M | F | M | F | M | F |
| **All cancers** | | | | | | | | | | | | | | | | | | | | |
| Lung | | | | | | | | | | | | | | | | | ■ | ● | | |
| Colorectal | | | | | | | | | | | | | | | | | ■ | ● | | |
| Breast | | | | | | | | | | | | | | | | | | ● | | |
| Pancreas | | | | | | | | | | | | | | | | | ■ | ● | ■ | ● |
| Prostate | | | | | | | | | | | | | | | | | ■ | | | |
| Non-Hodgkin lymphoma | | | | | ■ | ● | | | | | | | ■ | ● | ■ | ● | ■ | ● | ■ | ● |
| Leukemia | | | | | | ● | | ● | | | | | ■ | ● | ■ | ● | ■ | ● | ■ | ● |
| Bladder | | | | ● | ■ | ● | ■ | ● | | | | | ■ | ● | ■ | ● | ■ | ● | ■ | ● |
| Stomach | | | | ● | ■ | ● | ■ | ● | | | | | ■ | ● | ■ | ● | ■ | ● | ■ | ● |
| Brain | | | | | ■ | ● | ■ | ● | | | | | ■ | ● | ■ | ● | ■ | ● | ■ | ● |
| Esophagus | | | | ● | ■ | ● | | ● | | | | | ■ | ● | ■ | ● | ■ | ● | ■ | ● |
| Kidney | | | | ● | ■ | ● | ■ | ● | | | | | ■ | ● | ■ | ● | ■ | ● | ■ | ● |
| Ovary | | | | | | | | | | | | | | ● | | | | ● | | ● |
| Multiple myeloma | | | | | ■ | ● | ■ | ● | | | | | ■ | ● | ■ | ● | ■ | ● | ■ | ● |
| Oral | | | | ● | ■ | ● | ■ | ● | | | | | ■ | ● | ■ | ● | ■ | ● | ■ | ● |
| Melanoma | | ● | ■ | ● | ■ | ● | ■ | ● | | | | | ■ | ● | ■ | ● | ■ | ● | ■ | ● |
| Liver | | | | ● | ■ | ● | ■ | ● | | | | | ■ | ● | ■ | ● | ■ | ● | ■ | ● |
| Body of uterus | | | | | | ● | | ● | | | | | | ● | | ● | | ● | | ● |
| Larynx | | ● | ■ | ● | ■ | ● | ■ | ● | | ● | | ● | ■ | ● | ■ | ● | ■ | ● | ■ | ● |
| Cervix | | | | ● | | ● | | ● | | | | | | ● | | ● | | ● | | ● |

M = males; F = females. BC = British Columbia; AB = Alberta; SK = Saskatchewan; MB = Manitoba; ON = Ontario; QC = Quebec; NB = New Brunswick; NS = Nova Scotia; PE = Prince Edward Island; NL = Newfoundland and Labrador.

* Nordpred Power5 regression model is the default for all provinces except when the average annual deaths for the most recent five years is less than or equal to 50, when the five-year average estimate is the default.

**Note:** For territories (not shown), five-year average method was used for "All cancers" because of small numbers.

# APPENDIX III: Previous special topics, abbreviations and indices

## Previous special topics

Special topics are related to current or ongoing issues in cancer surveillance or cancer control. In particular, they aim to provide an in-depth look at the Canadian context. The following previous special topics are available at www.cancer.ca/statistics:

| | |
|---|---|
| **2011** | Colorectal cancer |
| **2010** | End-of-life care<br>Cancer in depth: Esophagus cancer<br>Cancer in depth: Kidney cancer |
| **2009** | Cancer in adolescents and young adults (15–29 years) |
| **2008** | Childhood cancer (ages 0–14) |
| **2007** | Breast cancer |
| **2006** | Progress in cancer control: screening |
| **2005** | Progress in cancer prevention: modifiable risk factors |
| **2004** | International variation in cancer incidence, 1993–1997<br>Economic burden of cancer in Canada, 1998 |
| **2003** | Non-Hodgkin's lymphoma |
| **2002** | Cancer incidence in young adults<br>Five-year relative cancer survival in Canada, 1992 |
| **2001** | Colorectal cancer |
| **2000** | Progress in cancer control |
| **1999** | Factors contributing to the population burden of cancer incidence and mortality<br>A new national cancer surveillance system for Canada |
| **1998** | International comparisons |
| **1997** | Ten years of Canadian cancer statistics |
| **1996** | Prostate cancer<br>Direct costs of cancer in Canada, 1993<br>Evaluation of cancer estimates: 1987–1991 |
| **1995** | Prevalence of cancer<br>Colorectal cancer |
| **1993** | Female breast cancer |
| **1991** | Smoking and lung cancer<br>Cancer among the Inuit and Indians |
| **1990** | Cancer of the female breast and genital organs – recent trends<br>Hodgkin's disease and cancer of the testis<br>Cancer mortality by income quintile<br>Economic cost of illness in Canada<br>Cancer control |
| **1989** | Cancer incidence and mortality: an international comparison |
| **1988** | Tobacco consumption from smoking and mortality from lung cancer<br>Cancer mortality: an international comparison |

## Abbreviations

| | |
|---|---|
| **AAPC** | Average annual percent change |
| **APC** | Annual percent change |
| **ASIR** | Age-standardized incidence rate |
| **ASMR** | Age-standardized mortality rate |
| **CCR** | Canadian Cancer Registry |
| **CCS** | Canadian Cancer Society |
| **CI** | Confidence interval |
| **CVS: D** | Canadian Vital Statistics – Death database |
| **DCO** | Death certificate only |
| **HBV** | Hepatitis B virus |
| **HCC** | Hepatocellular carcinoma |
| **HCV** | Hepatitis C virus |
| **ICCC-3** | International Classification of Childhood Cancer, Third Edition |
| **ICD-10** | International Statistical Classification of Diseases and Related Health Problems, Tenth Revision |
| **ICD-O-3** | International Classification of Diseases for Oncology, Third Edition |
| **NCIRS** | National Cancer Incidence Reporting System |
| **NMSC** | Non-melanoma skin cancer |
| **PHAC** | Public Health Agency of Canada |
| **PSA** | Prostate-specific antigen |
| **PYLL** | Potential years of life lost |
| **RSR** | Relative survival ratio |

## Index of tables and figures

### Tables

## Appendix tables



## Figures